The Research, Design and Development of a prototype Liquid Nitrogen Cryotherapy Device combining Electrical Stimulation and Heat.

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Ricardo Real

ABSTRACT

With a growing consumer driven cryotherapy market and its widespread applications in the medical industry a leading British cryotherapy clinic and equipment distributer have been researching the potential benefits to health and wellbeing of a novel procedure combining localised cryotherapy with electrical stimulation and heat. The project oversaw the development of a proof of principal prototype to allow further testing and technical development with a view to manufacture. Detailed in the project report is the research into multiple systems including a framework, heating system, Liquid Nitrogen pump and bodywork. An initial working proof of principal prototype was developed establishing an architecture for the combined machine considering function and user ergonomics.

ACKNOWLEDGEMENTS

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1 Introduction

The term Cryotherapy was derived from the Greek, 'Cryo' meaning cold and therapy meaning cure with its uses as a medical treatment documented as early as the 17th Century. Most prominently Cryotherapy is employed as a surgical treatment acknowledged by medical professionals as Cryosurgery. Used in the destruction of abnormal or diseased tissue and the dermatological treatment of skin conditions such as Warts, Solar Keratosis and Moles as a low risk, rapid and efficient outpatient procedure.

Historically, the properties of cold water submersion and Ice compression have been explored for their benefits to health including: Improved recovery, slow cell aging, decreased pain and muscle spasms and general wellbeing, thus, leading to the development of technologically enhanced Cryotherapy products including localised Cryotherapy units and whole body Cryo chambers; exposing patients to regulated Liquid Nitrogen vapour at a constant temperature of up to -186°C for a short period of time relative to the treatment type and area.

With a growing body of research into cryogenic technology and its widespread applications in the medical industry a British cryotherapy clinic and equipment distributer have been researching the potential benefits to health and wellbeing of a procedure combining localised cryotherapy, in which a jet of refrigerated Nitrogen gas is locally applied to alleviate symptoms of injury such as pain and inflammation, with Electrical stimulation, a procedure widely used in the management of pain and short term pain relief.

The company having successfully conducted a preliminary research study into the physiological benefits of a combined procedure at London South Bank University are

now looking to develop a prototype device to further explore the technical and commercial feasibility of a combined unit meeting the demands for novel procedures and devices in a growing consumer healthcare technology market.

The project aims to establish a set of parameters for the design of a combined unit through the research driven development of an initial working proof of principal prototype; further exploring the relationship between form and function in defining a configuration of components optimised to communicate use with user and environment.

The report provides an overview of the research and development of multiple systems in the delivery of a combined unit, particularly the development of an optimised rolling framework, a heating system and electrical stimulation configuration with further additional work detailing the research and development of a novel Liquid Nitrogen vapour filtering pump and its potential for Intellectual Property (IP) protection.

2 Background Research

This section of the report aims to introduce the research problem and outline a structured approach to project development. This chapter includes the following sections:

- Project Brief
- Methodology
- Explorative problem study
- Specifications for design

2.1 Methodology

A product development methodology was adopted to manage research and development at both organisation and project level. The methodology established a framework for structured product development, outlining an integrated approach to the management of quality and innovation.

2.1.1 Product Development Methodology

The British Standard BS 7000-2: 2008 Guide to managing the design of manufactured products from the BS 7000 Design Management System was selected to manage project research and development. (BSI - British Standards Institution, 2008)

The BS 7000-2 methodology was identified as an appropriate strategy for new product development within the projects scope through its integrated approach to design. Implementing an active framework to consider standards, product lifecycle and consumer needs in the definition of a new product.

Key features of the BS 7000-2: Methodology;

- Infrastructure to manage risks and meet standards.
- Research into consumer needs and market positioning.
- Promotion of environmentally sensitive design.
- A system for managing the design of manufactured products.
- Emphasis on frequent review and objective assessment.

Figure 1; below shows the BS 7000-2 approach to systematic project planning. The framework outlines elements to be considered in the proposal of a new product; thus,

prompting quality initial research to identify areas of opportunity and the potential to translate opportunity through innovation into commercial success.

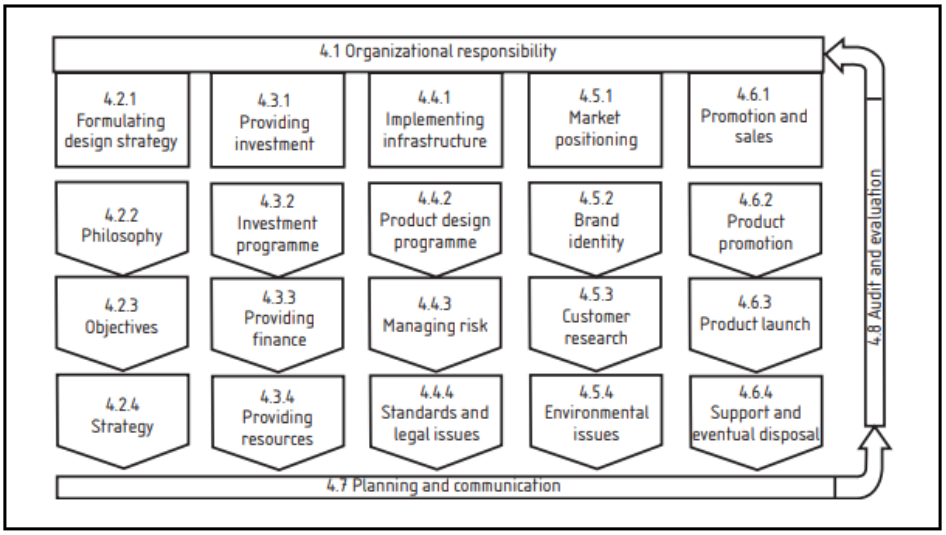


Figure 1 BS 7000-2: 2008, figure 3: Organizational elements of responsibility for product development, 2008

The standard is further applicable to the project though its outline of a phased product development methodology at project level.

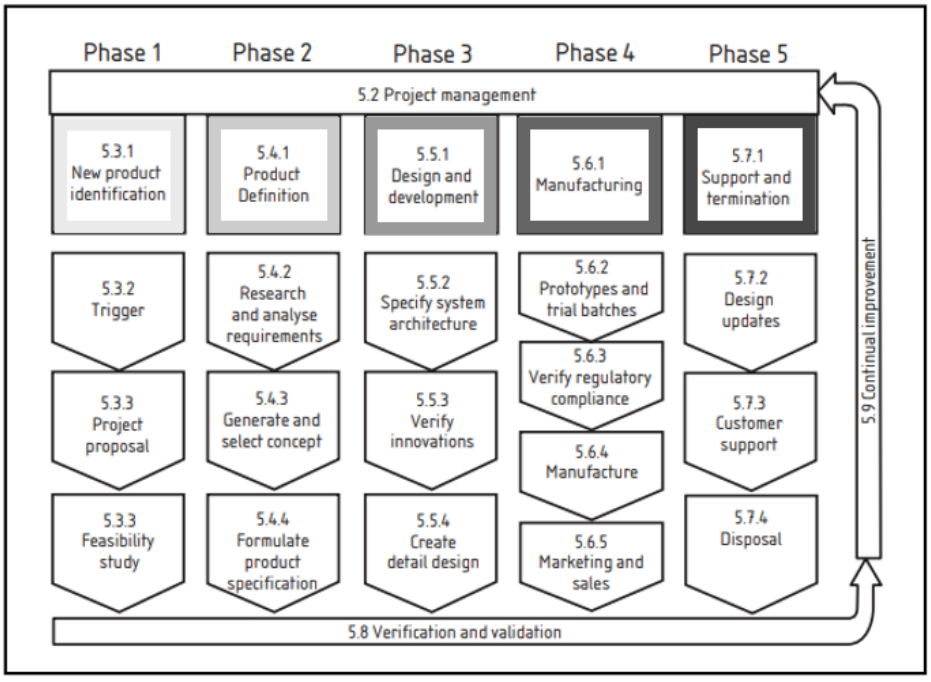


Figure 2 BS 7000-2: 2008, figure 9: The design process at project level, 2008

Figure 2 above titled "*the design process at project level"* proposes a method for managing new product delivery through conception to manufacture. A colour coding was applied over the table connecting this report to relative phases of the BS design process system.

2.1.2 Research Methodology

Given the multi-disciplinary nature of the project a mix of research methods were used where appropriate in the collection of data for product development. Methods including ethnography, observation, one-on-one interview and case study were used to gather qualitative data to build an understanding of the research problem through an exploration of the product/s and user and relative environment.

Quantitative methods of research such as the measurement and comparison of variables in engineering data were widely applied through phases of design engineering, with tools including system flow charts and analytical optimisation informing development.

2.2 Project Proposal

Following a study into the potential health benefits of a combined Cryotherapy and Electro muscle stimulation procedure, the School of Engineering at London South Bank University was approached to develop a proof of concept prototype.

CRYOSTIM - RESEARCH AND DEVELOPMENT PROPOSAL BRIEF:

Investigation of the Potential health benefits from combined application of Cryocooling and Electro Muscle Stimulation.

I. Aims

1. To study the physiological responses to treatment with current technology combining cryocooling and electrical muscle stimulation.
2. To develop a proof of concept prototype of a combined Cryocooler and electrical muscle stimulator.
3. To assess the physiological performance of the combined unit with the view to optimise the delivered health benefits.
4. To identify the potential for IP and exploration and to define the specifications for manufacture.

II. Work Plan and deliverables

1. **Proof of concept**
   a. Objective – To identify physiological effects of Cryotherapy with and without electrical stimulation. The performance of current technology will be investigated based on induced changes in key relevant measures of body composition and physiology including whole-body and segmental tissue composition (bioelectrical impedance method) thickness of subcutaneous fat layer (calliper or ultrasound doppler technology); subcutaneous blood flux and temperature (laser doppler monitoring), energy expenditure (gas exchange method)
   b. *Deliverable* – a specification for the combined system.

2. **Prototype Development**
   a. Objective – To develop a proof of principal prototype that combines cryocooling and electrical stimulation. This prototype will be based on criteria identified by the proof of concept study.
   b. *Deliverable* - a combined unit.

3. **Evaluation and feasibility**
   a. Objective – to evaluate the effectiveness of the prototype unit using physiological and metabolic outcome measures in order to: (i) validate the new combined machine and investigate its operational safety and reliability; (ii) identify the potential to produce health benefits (e.g. tackle obesity and metabolic disorders)

4. **Exploration**
   a. We will provide a specification for a new machine and the potential for exploration.

Figure 3 London South Bank University CRYOSTIM research project brief

Figure 3 above was presented as the initial research and development brief. The document outlined aims and deliverables for the project across disciplines. The following points highlight the scope for research within the School of Engineering.

- To develop a proof of concept prototype of a combined cryocooler and electrical muscle stimulator.
- To identify the potential for IP and exploration and to define the specifications for manufacture.
- Objective – To develop a proof of principal prototype that combines cryocooling and electrical stimulation. This prototype will be based on criteria identified by the proof of concept study.

The above points formed a basis for initial background research activity, prompting general investigation into Cryocooling and Electronic Muscle Stimulation through a mix of research methods explored in the following introductory research section.

2.3 Project Planning – Gantt Chart

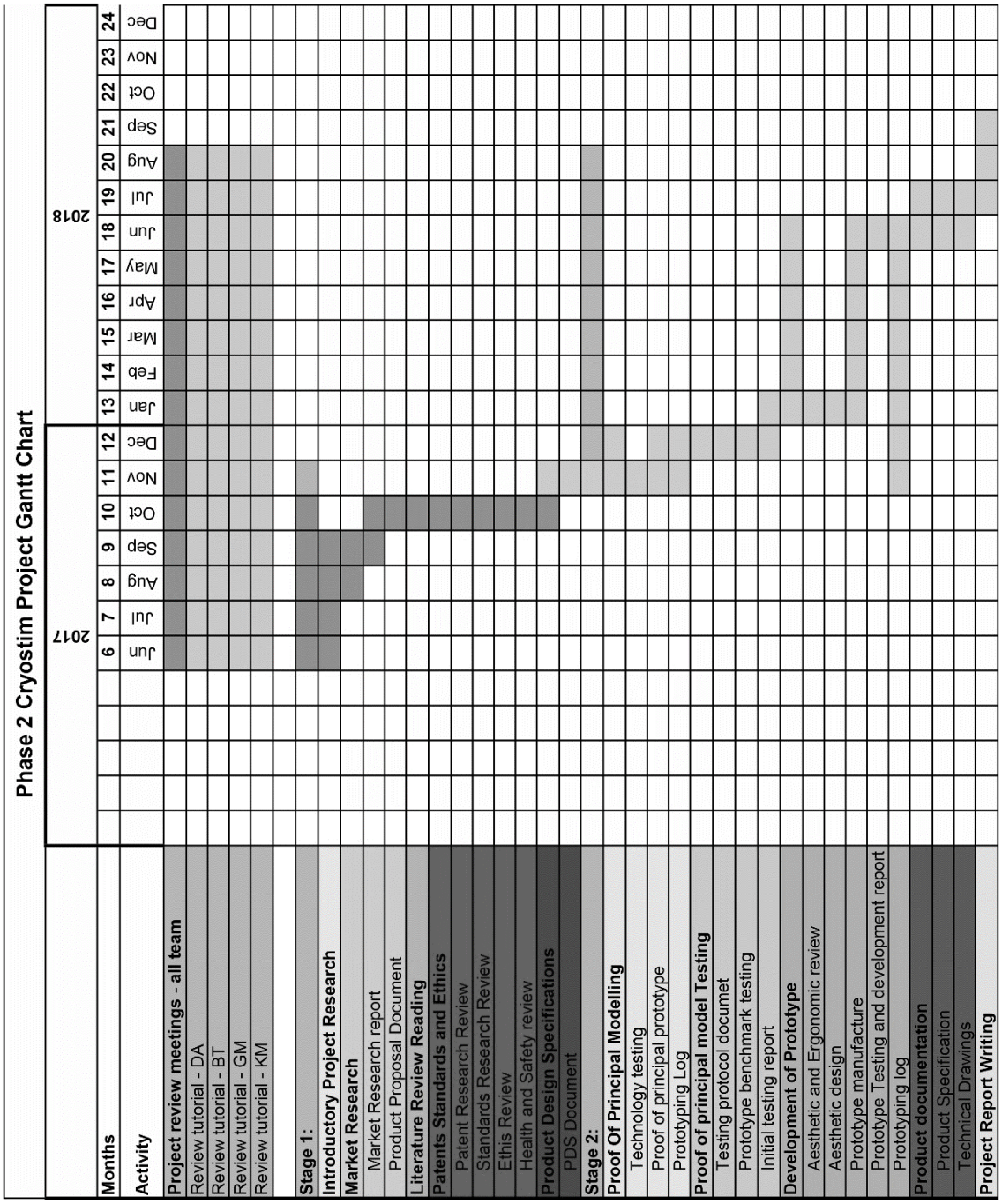


Figure 4 Project Gantt Chart

2.4 Research

This section of the report documents initial research activity and findings. The research activity outlined aims to explore the initial brief, defining a design specification document to implement goal driven product development throughout the project.

The research methods consist of the following elements;

- Literature review
- Ethnographic research
- Market Research
- Case Study
- Client interview

2.4.1 Literature Review

This section reviews literature published in the fields of Cryotherapy, Electrical Stimulation and procedures combining both. The literature review aimed to identify opportunities for new impactful research; further establishing a technical specification for a proof of concept prototype.

Literature was reviewed and documented with commentary into a literature database attached in the appendix of this report.

2.4.1.1 Cryotherapy

The reduction of skin temperature has been documented throughout history as a treatment for muscle injury. Hippocrates of ancient Greece gives mention to cold treatment and its therapeutic effects circa 470-370BC. The term cryotherapy however, was first introduced in 1908 by Pursey, describing physiological treatments with very low temperatures. (Galiuto, 2016)

Presently the term cryotherapy is used to group different modalities of treatment aimed at lowering the skin surface temperature around an injury site.

A local temperature reduction of between 10-15°C has been observed by researchers to successfully relieve local pain (analgesia), lower the metabolism, promote vasoconstriction and decrease inflammatory reaction. (Galiuto, 2016)

Currently a range of cryotherapy procedures are outlined, however, there is debate as to their efficacy. A study conducted into the effects of traditional cooling methods including: ice pack, ice massage and cold-water immersion (CWI), identifies CWI to have the greatest therapeutic effect, suggesting the larger coverage area of CWI as key to reducing motor nerve conduction and therefore symptoms of injury (Herrera , et al., 2010)

Recent technological innovation alongside the developing Liquid Nitrogen market has introduced novel cooling technologies to the cryotherapy marketplace. These technologies include: localised Cryotherapy, in which Liquid Nitrogen vapour reaching up to -170°C is applied to target a problem area, and, whole body cryotherapy, exposing

the user to refrigerated nitrogen vapour (-120°C) for a period of between 3-4 minutes in a cooling chamber, as a therapy for a range of conditions.

A 2015 meta-analysis aimed to critically evaluate novel cooling applications comparing local Cryotherapy with traditional cooling modalities. It was observed cold air applications (Liquid Nitrogen vapour) to have less of a therapeutic effect in comparison to ice pack and CWI treatments, concluding; "cold air applications probaly do not cool as deep as cold applications with direct contact to skin, and only effect skin temperature". The publication further discusses the role of adipose thickness (fat layer) in cooling, outlining scope for the study of an algorithm to calculate ideal cooling temperature from biometric input. (Hohenauer, et al., 2015)

A further study into adipose thickness and cooling time observed an increase in cooling time as adipose tissue thickness increased; thus indicating a dramatic adjustment to cryotherapy duration is required to produce similar intra muscular temperature changes. "A 25-minute treatment may be adequate for a patient with a skinfold of 20mm or less; however, a 40-minute application is required to produce similar results in a patient with skinfolds between 21-30mm, whereas a 60-minute application is required for patients with skinfolds of 30 to 40mm." (Otte, et al., 2002)

The safety of procedures is discussed in a 2015 publication in the International Journal of Applied Research and raises concern for the application of very low temperatures, suggesting precautions be taken as "prolonged application at low temperature below $15°C$ intramuscular could have deleterious effects to injury recovery", with too cold a therapy causing serious side effects including nerve damage and frost bite. (Saini, 2015) Furthermore, it is noted that Adenovirus is capable of survival in Liquid Nitrogen

therefore “the same source of Liquid Nitrogen should not be used with different patients.” (Unger & Elston , 2017) Furthermore, the vaporisation of Liquid Nitrogen in procedures can rapidly displace oxygen in the environment, resulting in cases of death by Asphyxia from evaporated Liquid Nitrogen. (Kim & Lee, 2008)

A concept in the foreground of cryotherapy research is the combination of cold and compression as more effective than single cold application. Documented as a procedure lasting an optimal time of 10 minutes (Kuo, et al., 2013) in which an ice pack is affixed to an injury area using an elasticated strap or similar to apply pressure promoting deep intramuscular cooling.

The results show the application of external compression to have a greater effect on the rate of restoration of function then does the frequency and duration of Cryotherapy procedures. (Wilerson & Horn-Kingery, 1993) Presenting an opportunity to explore the effects of a procedure combining cryotherapy, compression and electrical stimulation.

2.4.1.2 Neuromuscular Electrostimulation

Electrical stimulation has been used in the management of pain as far back as 63 A.D. reported by Scibonius Largus that pain was relieved by standing on an electrical fish at the sea shore. (Jenson, et al., 1985)

Clinical interest in the use of electrical currents to manage and treat pain has developed since the mid-1960s along with the “Gate Control Theory” of pain control. According to the theory selective stimulation of nerve fibers could block, or "close the gate" on signals carrying the pain impulse to the brain. (Reeve & Menon, 1996)

Electrical stimulation has found applications across physical therapy including rehabilitation, physiotherapy, occupational therapy, and speech therapy with the procedure becoming accepted amongst its practitioners as a standard for the treatment of both chronic and acute pain. (Reeve & Menon, 1996)

An exploration of neuromuscular electrostimulation techniques identifies two principal applications for electrical stimulation. Transcutaneous Electrical Nerve Stimulation (TENS) found with varying degrees of effectiveness in the treatment of mild to moderate pain by blocking pain signals (Gate theory) and, Electronic Myostimulation / Electronic Muscle Stimulation (EMS) generating impulses from an electro stimulation device, mimicking the action potential from the central nervous system causing muscles to contract. (Heidland, et al., 2013) with uses cited in the sports science field as a complimentary technique for sports training. (Zatsiorsky & Kraemer, 2006)

The efficacy of electrical stimulation in post-exercise recovery was reviewed, identifying stimulation parameters for both high frequency electrical stimulation < 10 Hz (resulting in visible muscle contractions, EMS), and, low frequency electrical stimulation, between 50-100 Hz (delivering strong but comfortable muscle stimulation without muscle contraction, TENS).

The parameters for procedures in the studies reviewed range from 4 Hz to 120 Hz for durations of between 40 to 250 μs. (Babault, et al., 2011)

Although electro stimulation is widely practiced amongst clinicians, questions are raised as to its effectiveness in pain reduction and rehabilitation. A 12-week double blind study

comparing TENS to sham TENS (no TENS) in a working age population for chronic non-specific low back pain, observed the TENS group to have minimal improvements over the non-tens group. (Thiese, et al., 2013)

Further studies suggest little evidence other than limited use of TENS in medical procedures, concluding TENS wasteful if its optimum case/use has not been identified. (Reeve & Menon, 1996) These observations have prompted research into combined procedures to enhance the reported analgesic effects of a standalone electrostimulation procedure.

2.4.1.3 Combined Cryotherapy / Neuromuscular Electrostimulation

Following calls to research the potential to enhance the therapeutic effects of both cryotherapy and neuromuscular electrostimulation, a 1992 study into electrostimulation, cold and a combined procedure identifies a combination of electrostimulation with cold, or a simultaneous application of both electrostimulation and cold as having a greater analgesic therapeutic effect on patients than just cold treatment or electrostimulation. (Denegar & Perrin, 1992)

An investigation into the working principal behind combined transcutaneous electrical stimulation and Cryotherapy on femoral nerve activity (FNA) in rats further validates the potential improvements of a combined procedure. Researchers found the combination significantly attenuated the effects produced by transcutaneous electrical stimulation alone on nerve activity. (Santuzzi, et al., 2008)

The analgesic effectiveness of a combined cryotherapy electrical stimulation procedure was however reviewed on patients with chronic lower back pain and compared to isolated procedures, results indicated the combination to have no significant improvement over isolated procedures; although the study does claim all three therapeutic modalities to be individually effective in relieving chronic low back pain. (Abreu, et al., 2011)

A more recent 2017 study has looked to further explore treatment combinations to enhance pain relief, in particular the addition of local heat to cryotherapy and electrostimulation. The study outlines a method using a heat pad at a temperature of 40°C placed over electrostimulation electrodes to heat the local area throughout the duration of a procedure. Alternately, the same method was used applying a cold pack with a surface temperature of 10°C for comparison. A standard electrostimulation pulse setting of 100 Hz with a 200 μs pulse width was constant throughout the procedure with a total duration of 20 minutes. The study concluded "TENS simultaneously combined with local heat or cold does not provide a synergistic analgesic interaction compared with TENS alone". (Maeda, et al., 2017)

2.4.2 Client Interview

Following an initial review of the brief, an unstructured meeting was arranged with the client, 'Ice Health Cryotherapy Limited', at their London clinic to discuss the brief further. The meeting allowed for the working principle of a combined

procedure to be demonstrated and the existing Cryocooling/Electro Muscle Stimulation devices and procedures offered at the clinic to be reviewed.

At this stage an addition was made to the original brief, adding a method of local heating to the deliverable, thus redefining the proof of concept prototype as a unit combining **LOCAL CRYOTHERAPY, ELECTRICAL MUSCLE STIMULATION AND LOCAL HEATING.**

Figure 5 Technology currently used in practice (Left: METRUM CRYOFLEX CRYO-T ELEPHANT right: VIP ITALIA VIPLINE PLUS

The image above shows the devices currently used to deliver both independent and combined procedures at the clinic.

Figure 5 can further be referred to in clarification of the brief, presenting the technology specified by the client to be combined into a new mobile standalone unit. The prototype unit is to allow for both independent and combined Liquid Nitrogen cryotherapy /

Electrical Stimulation / Heat to be delivered as part of a pre-programmed/programmable cycle for further research into the optimal settings for a combined procedure.

Following the meeting a document was produced collating specifications for the functionality and design from the client; including features beneficial to a procedure, benchmark performance parameters, aesthetics and ergonomics.

MEETING NOTES

INITIAL MEETING

A write up of the notes for product specification taken during an initial meeting for the development of a prototype unit. The notes are categorised into Core Function (CF) / Auxiliary function (AF) / Design (D)

SPECIFICATION NOTE	CATEGORY
A prototype standalone unit combining Cryotherapy / Electro muscle stimulation / Heat in a compact footprint for clinical use.	CF
Independently deliver Liquid Nitrogen Cryotherapy procedures for between 15 – 45 minutes from a 35L Liquid Nitrogen dewar, at temperatures up to -170°C.	CF
Independently deliver range of EMS/TENS procedures including: Muscle toning / Slimming / Pain relief / Lymphatic drainage from both hand-held probe applicators and pads.	CF
Independently deliver heat to a local area of the skin (hairdryer example given).	CF
Sensors to accurately measure temperature at skin without contact (safety feature to prevent injury including frost bite).	AF
Mode of measuring the amount of Liquid Nitrogen in the tank.	AF
Adjustable Liquid Nitrogen flowrate speeds through nozzle (controlled through sensor skin temp reading).	AF
Ability to preprogram treatment procedures combining the three technologies.	AF
An interface to control the machine and monitor procedures real time through measurement of temp, settings, program and cycle.	CF
Ability personalise treatments from sensor readings / biofeedback.	AF
Adjustable distance measure from cryotherapy handle to skin.	AF
Ergonomically designed handles for EMS / Heat / CRYO.	D
Ergonomically designed for the clinic environment and user.	D
Aesthetic design for the clinical / medical environment.	D
Design explored for manufacture in batches.	D
On wheels for maneuverability in clinic / storage / portability.	AF

Table 1 - Initial meeting notes

The document above establishes an early specification for the project, informing subsequent introductory research, highlighting areas to further investigate.

2.4.3 Ethnographic Study

An ethnographic study was performed to interact with and observe a practitioner and device in their working environment. The study looked at the challenges posed by the environment and technology to a practitioner delivering a combined procedure.

The study was conducted in a treatment room frequently used at the Ice Health Cryotherapy clinic to deliver both combined and independent Cryo/EMS procedures.

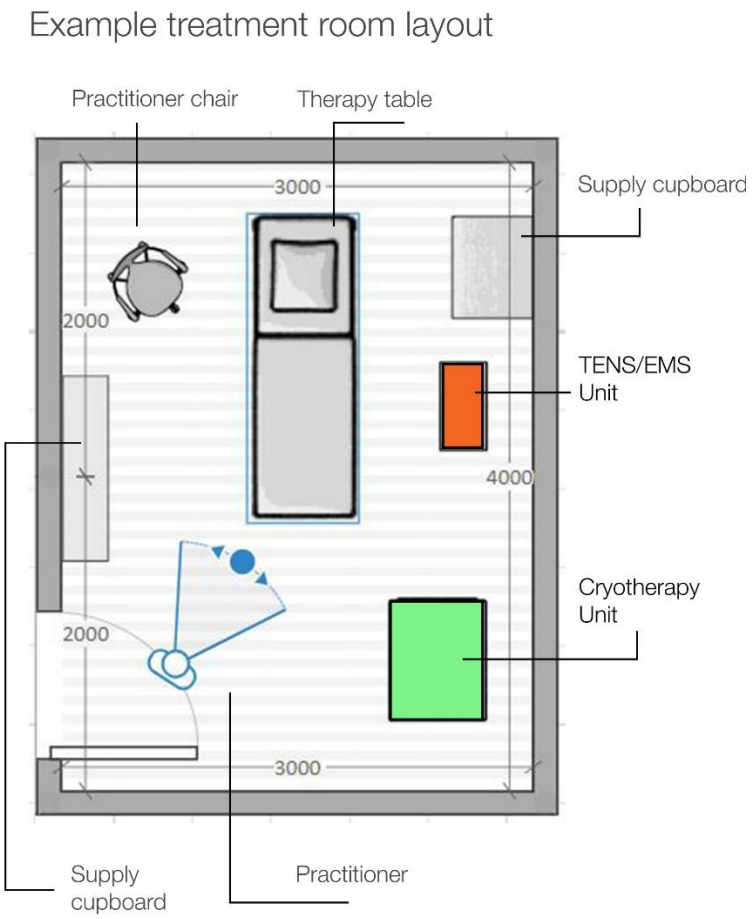


Figure 6 Room Layout Cryotherapy clinic example

Figure 5 above depicts the treatment room in which the study was performed. The room features a Central therapy table with Cryotherapy and TENS/EMS units adjacent, space for accessories/supply storage and a chair for the practitioner to optionally work from.

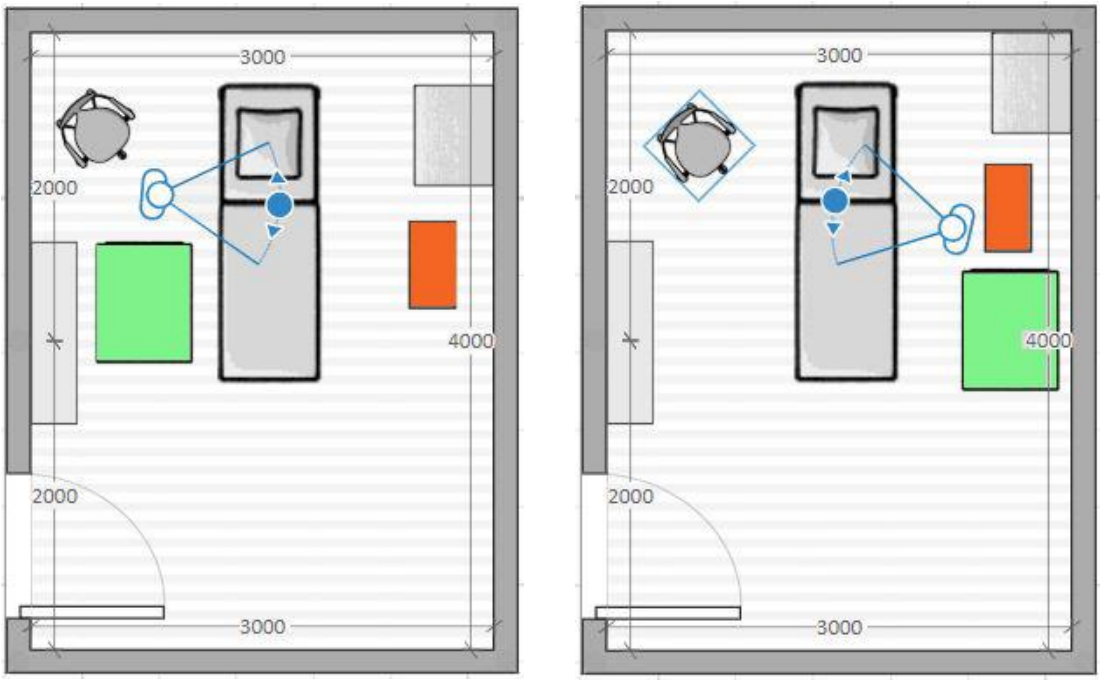


Figure 7 Clinic practitioner/machine configurations

An assessment of the possible working configurations of a current combined procedure highlight the impracticability in switching between isolated devices. For instance, figure 6, a left side procedure requires the practitioner reposition the cryotherapy device to the working area for comfortable use (as limited by the length of the hose). Whilst, being restricted by a grounded, non-mobile electrical stimulation unit.

The observations underline manoeuvrability and compactness as key components to the successful design of a combined device, allowing the practitioner to easily reposition the device to work around the patient and room layouts.

An image board featured below summarises the resultant findings of the ethnography study, including; appropriate use of warnings/safety symbols, simple hardware interfaces, ergonomics for prolonged use, and a large clear display interface all effecting the way a user interacts with the device.

Figure 8 Ethnography image board

2.4.4 Market Research

The market was researched, and a report produced looking at the Cryogenic health industry. The report aimed to better understand the characteristics of consumers, products and procedures driving the "Cryo" healthcare industry and the attitudes of consumers towards them.

The 'Phase II – Market research report' (attached in the appendix of this document) examined the market for opportunity; anticipating areas for future growth and the factors contributing to the success of a new product/market entrant.

Summarised in the following tables are findings from the market analysis.

Markets Opportunities	Strength
Demographic shifts and social change – Consumers embracing healthcare technology resulting in a rapidly growing consumer driven market.	5
Technology Advancements – Artificial intelligence, Machine learning, Big Data and the internet of things creating interest in health tech - new market opportunities.	5
Personalised Healthcare – Consumer attitudes shifting to personalised procedures preference.	5
Mobile Treatments – Consumers adopting mobile treatments enabled by mobile applications.	5
New Business Models – Redefined business models, creating a demand for product innovation allowing market growth and new business development.	4
Market Risks	**Strength**
Rapidly Changing Markets – Rapidly changing consumer driven markets and attitudes leading to shorter market trends and faster product turnover.	2
Empowered Consumers – Consumers shifting towards do-it-yourself alternatives through availability of online documentation.	2
Influx of Competitors – The markets strength could lead to more competition in the Cryogenic health sector.	2
Economic Conditions – Periods of slower market growth relative to the economic climate.	2

Table 2 Cryogenic Healthcare Market opportunity and risk – Market Research Report

Table 2 outlines the market opportunities and risks observed in the overall cryogenic healthcare and wellbeing market; encompassing procedures across the “cryo” category.

Two principal cryogenic procedures were found to be driving market growth, the procedures being:

- Cryolipolysis a body contouring procedure in which the application of cold is used to reduce local subcutaneous fat through adipose apoptosis.
- Cryotherapy a procedure aimed at relieving the symptoms of sporting/general injury and improving recovery post training.

A further analysis with a focus on the consumer and media attitudes was undertaken. Market data was collected and quantified allowing for comparative analysis of both procedures to identify areas presenting most market opportunity.

From the research a strong upward trend was identified in consumers adopting technology enabled procedures to deliver alternative non-invasive health and wellbeing treatments. However, the research also highlighted a lack of market innovation in the current cryogenic healthcare industry, with few products offering new procedures or novel combinations.

The table below from the market report investigates the tertiary industry i.e, the Clinics, Health Spas, Gymnasiums ect making up the demographic of potential future device consumer and their demands from new products.

Tertiary Sector needs from new product development

Consumer	Product needs
Tertiary sector – (health clinics, beauty clinics, spa's, therapists, mobile therapists, salons)	Offer significant innovation or marketability to compete with existing technology.
	Present value as an investment capable of increasing revenues through procedure sales; contributing to business growth.
	Backed by research and development increasing consumer confidence and procedure marketability therefore adoption.
	Developed alongside emerging social trends, encompassing the market direction and consumer attitudes to deliver disruptive products and present potential for future market growth and segmentation.
	Designed for their environment, durable low maintenance and safe; meeting relevant market regulations.

Cryolipolysis

Consumer	Product needs
Tertiary Sector Cryotherapy - (clinics, health and wellbeing centres, Gyms, Spas, clubs)	Offer significant innovation or marketability to compete with existing technology.
	Present value as an investment capable of increasing revenues; contributing to business growth.
	Backed by research and development increasing consumer confidence and procedure marketability therefore adoption.
	Developed alongside emerging social trends, encompassing the market direction and consumer attitudes to deliver disruptive products and present potential for future market growth.
	Efficient
	Designed for their environment, durable low maintenance and safe; meeting relevant market regulations.

Cryotherapy

Table 3 Tertiary sector needs from NPD – Market Research Report

The findings from the market research above, further inform the development of the product specification document. Thus, ensuring future market trends and shifting consumer attitudes are considered in the proposal of a new product; leading to greater potential for longer product life in service and therefore value and quality from new product development.

On the following page an infographic summary of the market research in terms of consumer attitudes is presented. The figure provides a simple metric for emerging trends in the cryogenic healthcare market, with more weighting applied to the stronger consumer driven market attitudes.

Figure 9 Cryogenic market buzzwords

2.4.5 Case Study

The study was presented alongside the market report reviewing business activity contributing to market success. The case study looking into a successful Cryogenic healthcare business, their practices and products revealed 5 key factors to have positively impacted market success.

The study reviewed market leader Zeltiq's proprietary cryolipolysis procedure, Coolsculpting®; acquired by Allergan, owner of Botox® for $2.48 Billion in February 2017.

Figure 10 Case Study factors of success – Market Research Report

The complete case study and review may be found featured in the market report attached in the appendix. (It should however be noted that the clinical research and development of a novel procedure (cryolipolysis) and its FDA approval are the leading contributions to market success)

2.5 Research Findings

Independently, cryotherapy and electrical stimulation have been found to have varying therapeutic effects on its users with applications ranging from the management and treatment of pain to improving post exercise recovery.

Current research into combined procedures identify potential for improvement in procedure efficacy over independent applications, however, a significant gap in the research is present in the definition of the optimal parameters for a combined procedure.

With a growing demographic of consumers looking for technology enhanced healthcare procedures and strong industry demand for new marketable procedures and devices, there is scope for further research into a combined procedure to address both the gap in literature and industry demand for novel research backed procedures.

The research highlights the significance of compact manoeuvrable space saving solutions designed around the product environment as key to market success, however a consumer trend is emerging in 'do it yourself' therapy favouring lower cost alternatives that can be used from home or as part of a home healthcare toolkit.

As a final note, awareness and caution are building around the use of cryogenically low temperatures in healthcare procedures, in particular procedures using Liquid Nitrogen. Cases of injury including nerve damage and frost bike have been reported along with incidents resulting in death; should Liquid Nitrogen be the modality of cooling, measures should be implemented through design to safeguard patient and practitioner.

2.6 Design Specification

The specification of a new product was informed by the prior research activities. The following specification outlines detail for the design, including technical specifications, environmental factors, ergonomics, aesthetic, maintenance and health and safety.

The PDS headings are based on the PDS of Pugh, 1990.

1. **Performance**

   - The device must be able to deliver a jet of refrigerated nitrogen gas at variable flow rates to reduce skin temperature by 10-15°C as outlined by research. With a target temperature cold stream of up to –170°C defined by the client.
   - Allow continuous use up to 1hr without refilling.
   - Be able to deliver a range of Electrical Stimulation procedures from 4 Hz to 120 Hz for between 40 to 250 µs.
   - Be able to apply heat around 40°C to a local area.
   - Run on both 120V – 240V
   - Have sensors to accurately measure skin temperature, further allowing sensor controlled cold temperature algorithm through software development.
   - Feature a display unit to allow for software driven control.
   - Withstand maximum LN load to a relevant safety factor, and forces put upon the device to manoeuvre when fully loaded.
   - Be able to measure the amount of Liquid Nitrogen real time throughout a procedure. with a minimum cut off requirement.
   - Monitor Oxygen Level in room
   - Measure distance from a target surface from applicator end.

2. **Environment**

   The product is to be used in an indoor clinical/medical environment, with temperatures between 18-30°C at an average humidity of 40-50%. Electronics should be appropriately enclosed and protected against moisture.

3. The device is to be predominantly used in a treatment room however moved when necessary to other areas of a healthcare facility along smooth, flat surfaces. The areas in which the device is to be used risk oxygen depletion that can lead to death by asphyxiation if not correctly ventilated, and, a nitrogen rich environment for machine operation. The device is likely to be handled with care by informed users having read the product manuals/documentation.

4. **Life in Service**

   An expected life in service of 15+ years through design for maintainability, with a dormant period of 50+ years in stable storage conditions.

5. **Maintenance**

   The machine would require refilling with 35L of Liquid Nitrogen from a supply tank by the practitioner or technician who should be trained in the safe handling of hazardous substances and take appropriate safety measures in refilling.

6. **Target Product Cost**

   A forecast retail price of between £15,000.00 and £20,000.00 per unit in the current market based on procedure novelty (given positive treatment results) and intellectual property as value adding. With a target manufacture price per unit (in batches of 100 units) of £1,650.00 (excluding the Liquid Nitrogen Dewar vessel estimated at +£1,250.00 per unit) total machine cost £2,900.00 per unit.

7. **Competition**

   Currently no clinical devices are commercially available combining LN Cryotherapy, Electrical Stimulation and Heat. Existing procedures are offered independently either through clinics or alternatively low-cost home use devices such as ice packs and TENS units.

8. **Shipping**

   The device is to fit within the footprint of a standard UK pallet of 1200 x 1000mm protected by a hard shell (timber crate etc) and internal protective padding. Consideration should be given to the height of the packaged device to allow more

units stacked for transportation and warehousing. Shipped via freight, shipping container, independent units dispatched via large good courier with forklift.

9. **Packing**

   Only requires industrial freight packaging for transport and warehousing, using environmentally friendly materials such as recycled plastic pallets / timber crates from managed forests.

10. **Quantity**

    The product is intended for production runs of 100 units, allowing for a sufficient balance between unit manufacture cost/time and the demands of a growing international market. There is strong demand from the market for novel procedures, given appropriate marketing exposure and economic trading conditions.

11. **Manufacturing Facility**

    A manufacturer capable of full in-house production is recommended. The manufacturer should have appropriate certification e.g ISO 13485:3003 and testing capability. Some components may be manufactured to specification elsewhere /outsourced to reduce manufacture time and additional set up cost. Production is viable nationally however alternative manufacturers working to regulation within the European Economic Area should also be considered.

12. **Size**

    The size of the device is dictated by the size of the specified Dewar vessel, 35L, and factors of form for ergonomic use of the machine. The device should be kept as compact as possible following the ethnographic study and aim to cut material where unnecessary.

13. **Weight**

    The devices overall weight is dependent on the quantity of Liquid Nitrogen being held, the design should be optimised to the maximum Liquid Nitrogen capacity with an appropriate safety factor. Efforts should be made to minimise material

usage thus overall weight without compromising on function or overall quality.

14. **Aesthetics, Appearance, and Finish**

    The Aesthetic of the device should clearly communicate its functions for easy device adoption and usability. The Aesthetic should complement its clinical / medical environment, a functional design language with minimal hidden surfaces. Given the target consumer the device should convey a high product quality.

15. **Materials**

    Materials are to have a high specific strength where required i.e in structural components and minimal weight. Materials exposed to cryogenic temperatures should have appropriate properties for safe use under cryo conditions, for instance specific engineering polymers. A preference of smooth surface textures and materials non-reactive to liquid sterilising agents.

16. **Product Life Span**

    Used from new until a return has been made on the purchase cost, eventually replaced by a newer procedure/product. The device may then be resold on the second-hand market for a lower unit cost typically until either failure or upgrade, in either case resulting in obsolescence, from which the device can be broken down into its components for reuse or recycle.

17. **Standards and Specifications**

    CE markings must be applied to show compliance with applicable European medical device directives. The device or electrical systems used within the device must meet IEC 60601 standard for medical electrical equipment and systems (601 compliant) Devices with complex coding must meet a separate regulatory process specified in the IEC 62305 document. Risk management to medical devices ISO 14972. Symbols to be used with medical devices ISO 15223-1:2016. Electromagnetic compatibility EN-61000-3-2. ISO 13485.

18. **Ergonomics**

    The manoeuvrability of and around the device under varying loads is critical to successful ergonomic design, how the device responds to the user when in

movement or action for quality feedback. The design of components held to deliver procedures for comfort and control. The layout of device functions for simple interaction, allowing for intuitive use of different systems / components to the device.

19. **Customer and user**

    Customers including healthcare clinics, Spas, cryotherapy clinics, physical rehabilitation centres, physiotherapists, wellbeing centres, gyms, sporting facilities and clubs, military. Growing demographic of private users such as professional athletes or cryo enthusiastic individuals.

20. **Quality and Reliability**

    Systems designed and tested to relevant standards to ensure device reliability, built in maintainability to prolong life in use / quality. Outsourced components also to meet the relevant standards and regulations.

21. **Processes of manufacture**

    The majority of parts are to be manufactured using standardised manufacturing processes not requiring the development of new processes.

22. **Time scale**

    To deliver a frozen design specification and initial prototype unit within 16 months

23. **Testing**

    IEC 60601 medical safety testing. Testing to IECEE CB standards and CE marking.

24. **Safety**

    There is significant potential for product misuse and abuse, resulting in significant risk to users. The device should be operated by a user trained in the safe handling of cryogenic substances and used in a room meeting specified ventilation criteria to avoid oxygen depletion and the risk of death. The operator should also be trained to recognise the signs of overcooling and cold burns. Training and measures should be provided for the safe practice of refilling the device with LN.

The device should be regularly cleaned using liquid sterilising agents independent of environment.

25. **Company Constraints**

The company currently does not have the facilities to manufacture devices and thus would require the manufacture of products to be outsourced, furthermore the company has no inhouse design and engineering department, future design and development would also require outsourcing. These factors could be addressed by investing a small production site with skilled professionals capable of manufacturing and assembling components to relevant standard.

26. **Market Constraints**

The market is currently growing with consumers looking for new technology enhanced procedures, devices compatible with future consumer ideals such as smart healthcare and AI driven procedures prompted for strong market share.

27. **Patents, literature, and product data**

There are no patents on the combination of procedures as non-patentable, not meeting the new/novel/nonobvious criteria. The design of outsourced components may however be patented, for instance, the Liquid Nitrogen vapour pump, however the patent is limited to Poland. Searches were performed using the terms: Liquid Nitrogen Vapour pump, Cryotherapy pump, Cryogenic pump and liquid nitrogen pump, cold air jet.

28. **Political and social implications**

Health Canada issued a notice considering cryotherapy devices to be a potential health risk, requesting the manufacturer of devices stop the sale and immediately recall the unlicensed Class III devices, furthermore working with the Canadian border agency to prevent illegal importation of devices. Devices / procedures in the cryogenic health market may become restricted or subject to further regulation worldwide following the risk of injury and death to users. Publicity of such events could lead to a social shift away from low temperature cryotherapy to conventional ice-pack / ice bath procedures.

29. **Legal**

    Sufficient measures should be put in place to prevent injury or death to users. Documentation should be thorough and clear, and after sale support in place.

30. **Installation**

    Installation is to be performed by the user following a detailed installation and operation manual.

31. **Documentation**

    The device is to be supplied with instruction documentation on installation (including room set up) operation and maintenance. Other documentation provided: safety certificates, test certificates, health and safety warnings.

32. **Disposal and End-of-Life scenarios**

    The device can be broken down into its components for reuse or recycle. Repurposable parts should be chosen over custom / single use components where possible. Materials with specific properties should be identified to allow for effective recycling.

2.7 Concept Generation

The following pages explore concepts to meet the research defined criteria, including: Reducing skin temperature by 10-15°C, variable electrical stimulation settings and heat.

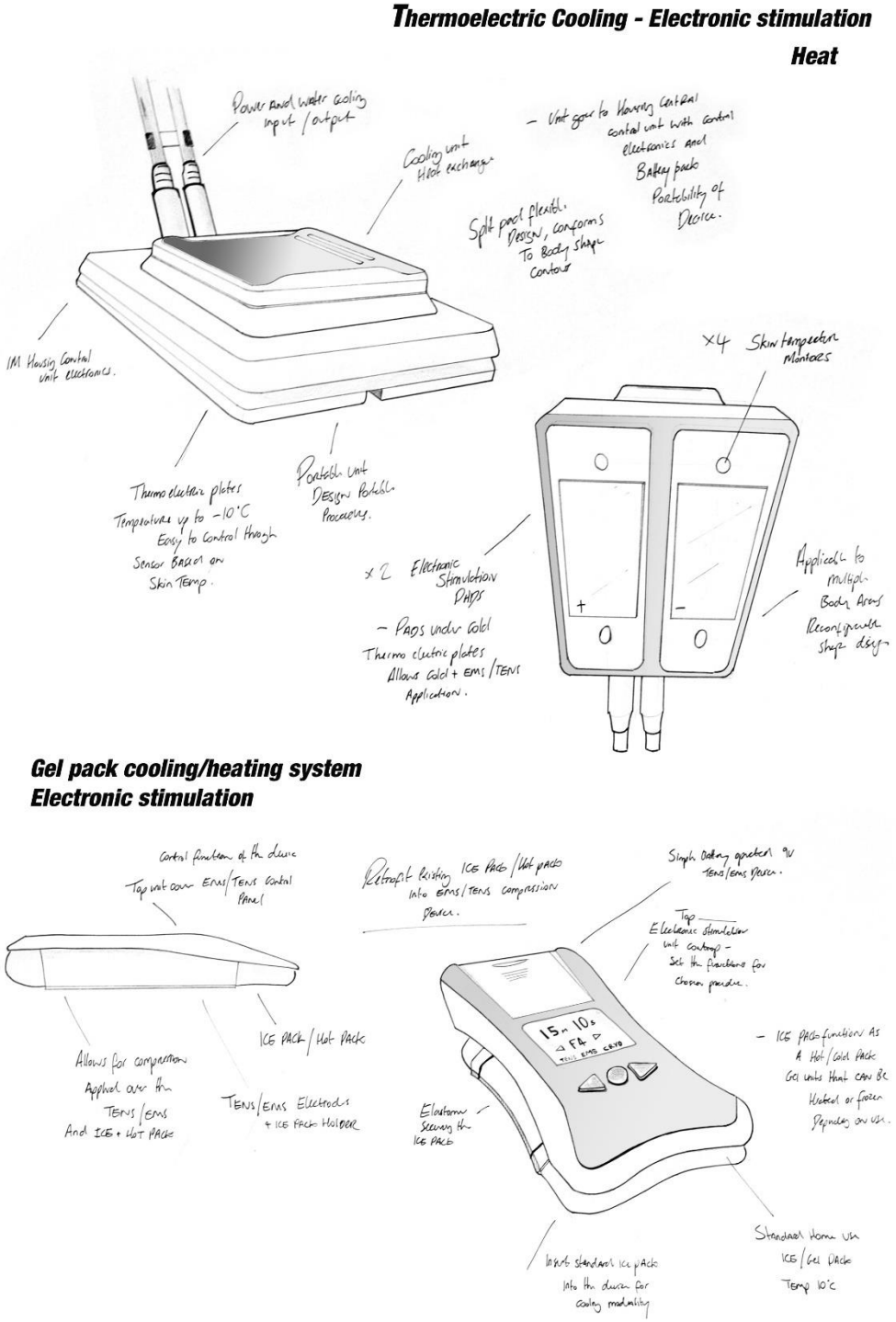


Figure 11 Ideation Sketches thermoelectric plates and gel pack cooling lower

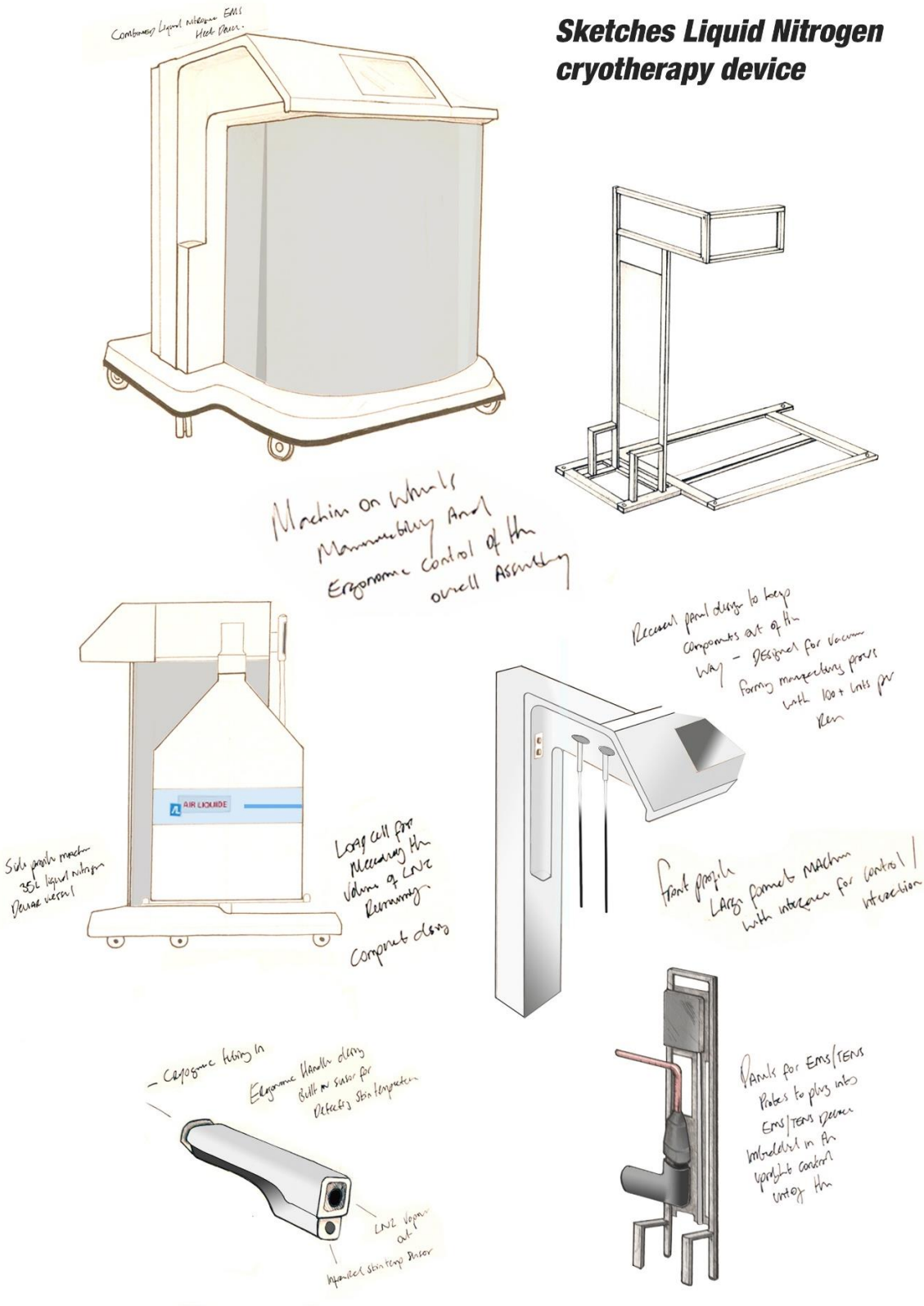


Figure 12 Liquid Nitrogen cryotherapy device ideation sketches

2.8 Concept Selection

Following sketch ideation, the top three concepts were further reviewed against a specification criterion evaluating the proposed concepts against a reference, being the current procedure set up.

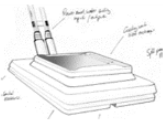
Pugh Concept Ranking Matrix				
Selection Criteria	 Reference			
1. Compactness	0	+	+	+
2. Treatment Efficiancy	0	+	0	+
3. Cost (Manufacture)	0	+	0	+
4. Profit margin potential	0	-	+	-
5. Ease of Use	0	+	+	+
6. Safety	0	+	0	+
	Sum +	5	3	5
	Sum -	1	0	1
	Sum 0	1	3	0
	Net Score	4	3	4
	Rank	2	2	1
	Continue	Yes	No	Yes

Table 4 Pugh concept ranking matrix

The results of the matrix ranking are displayed in table 4, with a scoring of: better than (+), the same (0) and worse (-) awarded respectively against the reference.

The prior research and concepts drawn from it were prepared in a folder to be presented to the client in a project meeting. **From the meeting the Liquid Nitrogen cryotherapy device was identified as the concept to further develop.**

2.9 Further Concept Development

A scale card model was developed around the dimensions of a 35L Air Liquide TR35 Liquid Nitrogen Dewar. The model defined key dimensions for the design along with an architecture for the arrangement of components within the framework.

Figure 13 Scale modelling card

The model was further used to study optimal ergonomic configurations and machine interaction in regards to touch screen interface and viewing angle.

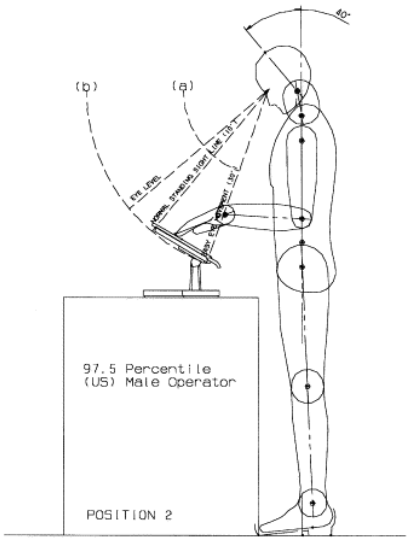


Figure 14 from the international journal of industrial ergonomics on the optimal viewing angle for touch screen displays; recommends, through anthropometric analysis, a viewing angle of between 30° and 55° off horizontal. (Schultz, et al., 1998)

The data was implemented in the card model and further evaluated.

Figure 14 Viewing angle for touch screen displays

Figure 15 Ergonomic form study

Following a review of the card model the data was translated into a CAD model (Autodesk Inventor) for further component architecture and structural analysis.

Figure 16 Analytical CAD model development

A preliminary aesthetic form for encasing of the machine was derived from the system architecture and modelled in blue foam. The components were produced on a CNC router, ensuring dimensional accuracy in the model for thorough evaluation.

Figure 17 Aesthetic blue foam modelling

The model was reviewed against the following basic criteria in the bullet points below and prepared for presentation to the client.

- Minimal surface area; reduced material usage, weight and surfaces for bacteria.
- Houses and protects internal components.
- A clinical aesthetic for the healthcare and wellbeing industry.
- Minimal floor footprint.

3 Design Development

The following section of the report outlines the process of design development through engineering analysis, prototype manufacture and testing. The section is subdivided into the three components;

1. Bare-bones development: A rolling chassis and mounted instruments.
2. The design and manufacture of a prototype Liquid Nitrogen vapour pump and subsequent components.
3. The design and manufacture of the machine bodywork.

3.1 Bare-bones Design: Framework, Electrical Stimulation and Heating

By definition bare-bones comprises only the basic or essential elements of something. This section outlines the development of a 'bare-bones' unit; a rolling chassis complete with mounted hardware.

Further detailed in this section is the design and development of components including heating and electrical stimulation assemblies, otherwise defined as 'Hardware'.

3.1.1 Framework Overview

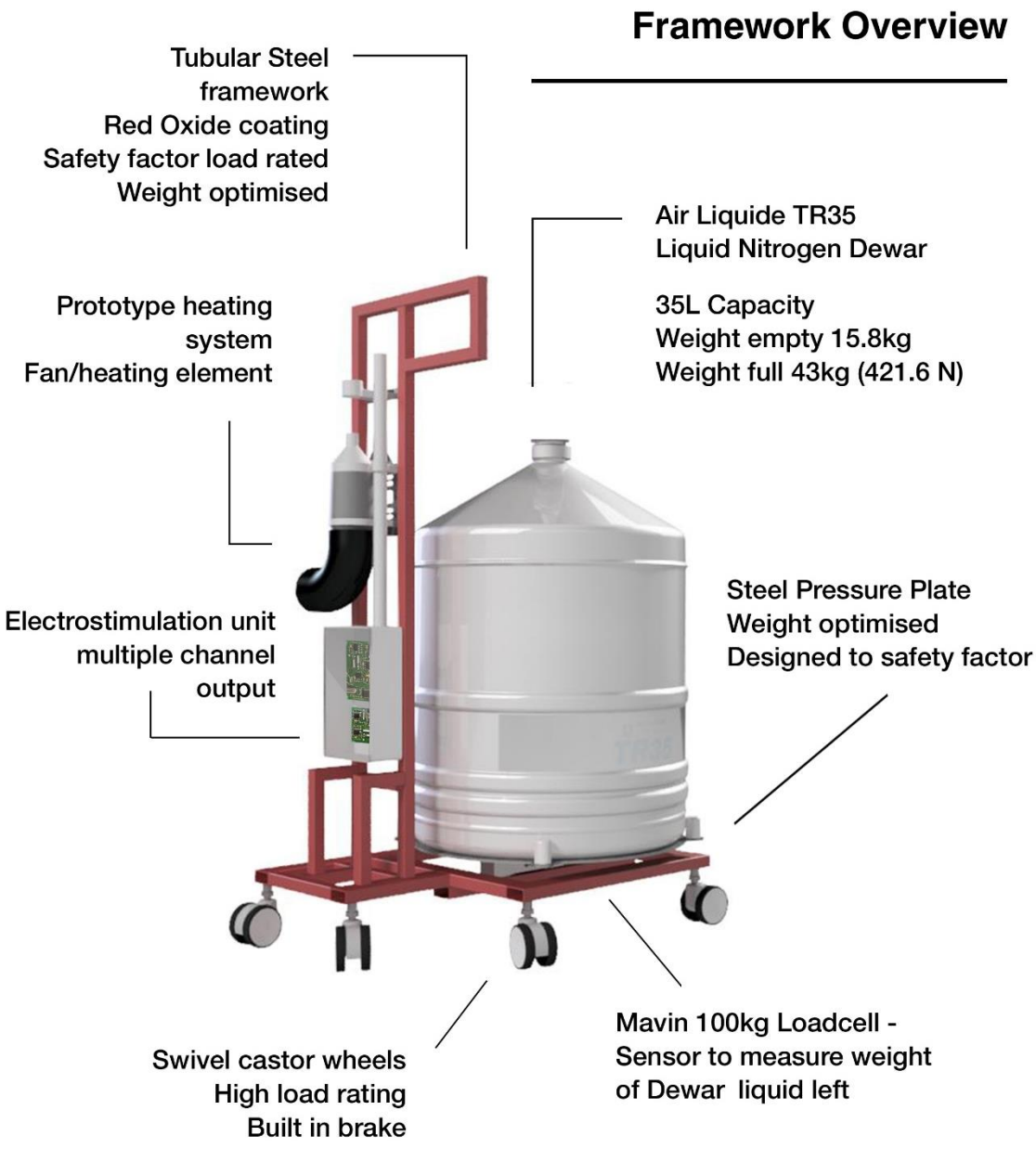


Figure 18 Framework Assembly Overview

3.1.2 Framework Design and Development

A framework was designed for the Air Liquide TR35 Liquid Nitrogen Dewar. The dimensions and loads of the vessel to capacity with Liquid Nitrogen (35L) are displayed in Figure 19 below.

Figure 19 Liquid Nitrogen Dewar

The objective of the framework design was to compact the footprint of the machine around the profile of the Dewar vessel, thus improving the ergonomics of the device, reducing material and overall cost.

Further considering compactness in the design, materials for the framework were reviewed for appropriate properties including strength to weight ratio (specific strength) cost and size.

	Modulus of Elasticity, E (GPa)	Ultimate Tensile Strength (MPa)	0.2% proof stress at Yield (MPa)	Elongation at Failure (%)	Fatigue Limit/ UTS (5x10 cycles)	Density (Mg/m - specific energy
Steels						
Medium Carbon	200	520	310	26	0.5	7.85
CrMo (AISI 4130)	200	1425	1240	12	0.5	7.85
Aluminum Alloys						
2024-T4	73.1	470	325	20	0.29	2.8
6061-T6	68.9	310	276	12	0.31	2.8
7075-T6	71.7	570	503	11	0.265	2.8
Magnesium	44	248	200	5 to 8	0.37	1.79
Titanium Alloys						
IMI 125	105 to 120	390 to 540	340	20 to 29	0.5	4.51
IMI 318	105 to 120	1000	900	8	0.55	4.42
Composites						
"S" glass-epoxy	90	3750	3450	3.5	0.16	2.63
HT graphite-epoxy	221	3600	2000	1.25	0.25	1.75
Boron-epoxy	250	1200	?	?	0.8	1.9
Boron-Aluminum	165	1025	?	0.65	0.7	2.4
Kevlar-49-resin	75	1380	?	2.75	0.7	1.45
Glass-nylon	2.3	59.9	59.9	14	?	1.18
Woods	12	100	60	?	?	0.67

Figure 20 Comparison materials table - (VanDragt, et al., 2000)

A study of materials found Steel box section to allow smaller tubular profiles to be used whilst maintaining high specific strength; therefore, increasing the amount of available space within the framework to further enable compactness.

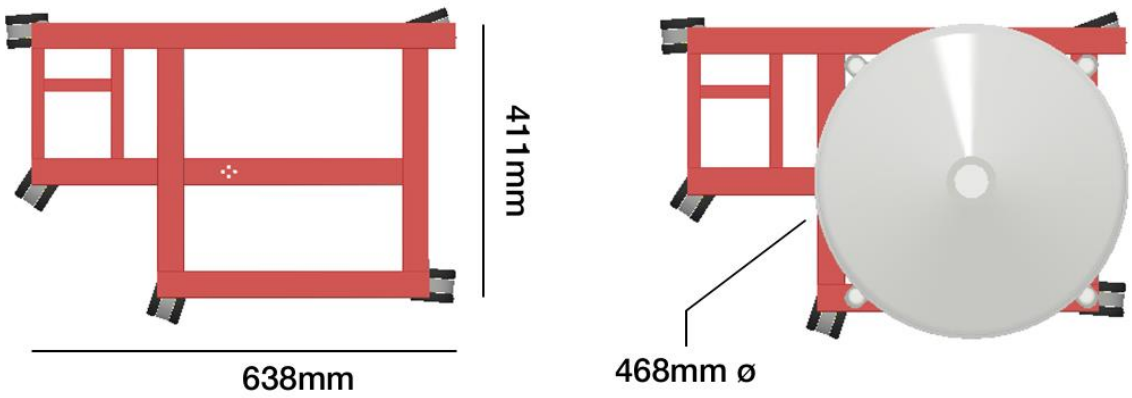


Figure 21 Lower Framework profile

Figure 21 above details the structure and dimensions of the lower rolling framework with mounting points for Load Cell and upright assembly. The development of the structure is documented through pages 4 to 19 of reference sketchbook 1.

Moments were taken around the lower framework to evaluate and optimise the rolling chassis, ensuring stability in the loaded assembly and therefore a factor of safety in compacting the framework profile whilst moving a Liquid Nitrogen vessel.

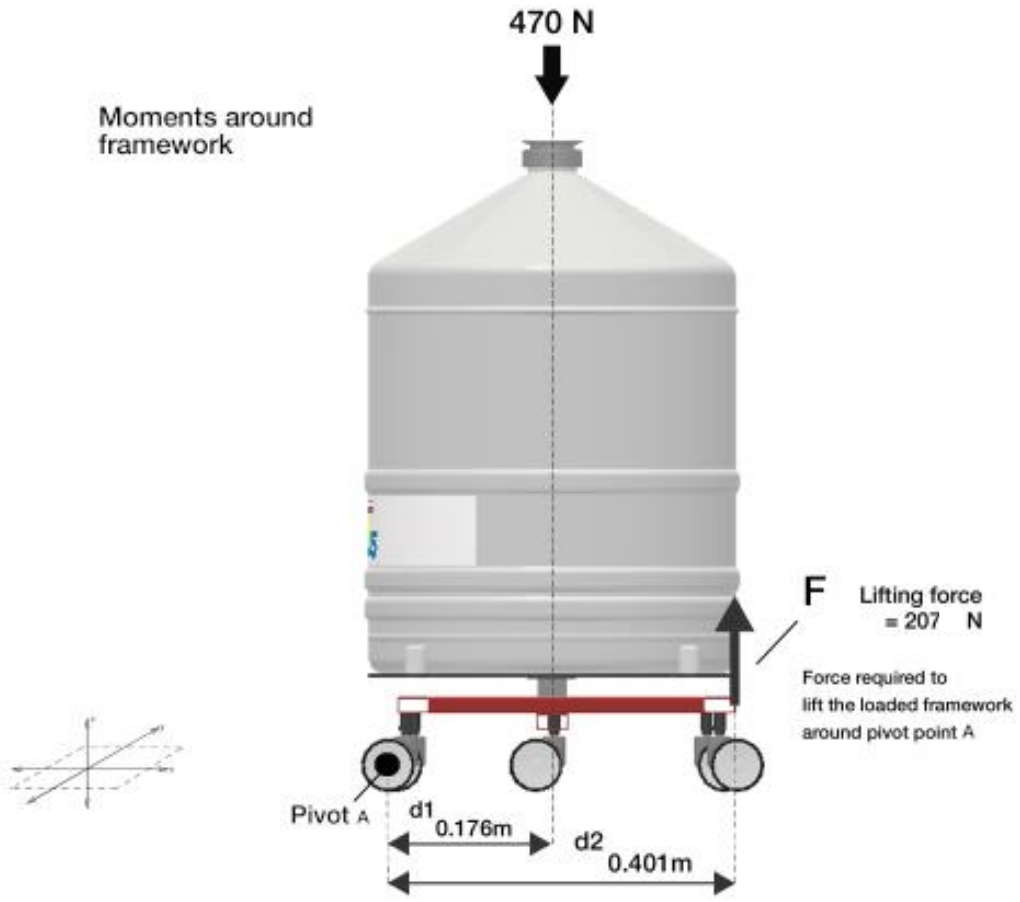


Figure 22 Moments around framework

The mechanical advantage at the point of applied force F around pivot A was calculated to allow variable loads when analysing the lifting force required at F.

$$\frac{d2}{d1} = \frac{0.401}{0.176} = 2.27$$

Where:

- d1 is the distance from pivot A the to the centre of mass through the loaded Liquid Nitrogen Dewar
- d2 is the distance from point A to the point of force application F

The force required to lift the load around pivot A in an anti-clockwise direction was calculated with a load of 470 N (47.95 kg) acting in the -z direction; accounting for a full 35L Liquid Nitrogen Dewar (43 kg) and a margin of 4.95 kg for Dewar mounted accessories.

The Force required to lift the load around point A =

$$W = mg = 47.95\ kg\ \left(9.8\ \frac{m}{s^2}\right) = 469.9\ N$$

Where:

- W is the force acting on the framework in Newtons
- m is the mass in kg
- g is the acceleration due to gravity 9.8 $\frac{m}{s^2}$

Rounding to 470 N and dividing the force by the mechanical advantage of the framework at the point of application, F, gives;

$$\frac{470\ N}{2.27} = \ 207\ N \quad Converting\ to\ kg \quad \frac{470\ N}{9.8\ \frac{m}{s^2}} = 21.1\ kg$$

Thus requiring 207 N applied anticlockwise (21.1 kg) to lift the load around pivot point A, equalling 44 % of the total load of the assembly. Showing the rolling chassis to be stable

under load, requiring significant applied force to tip over the assembly both static and in motion on a flat plane.

The rolling resistance of the framework was then calculated to define the force required to initially overcome the rolling resistance (F_{rr}) and further to accelerate the loaded framework to a walking pace of 1.4 m/s; with the results used to structurally analyse and optimise the design of the framework.

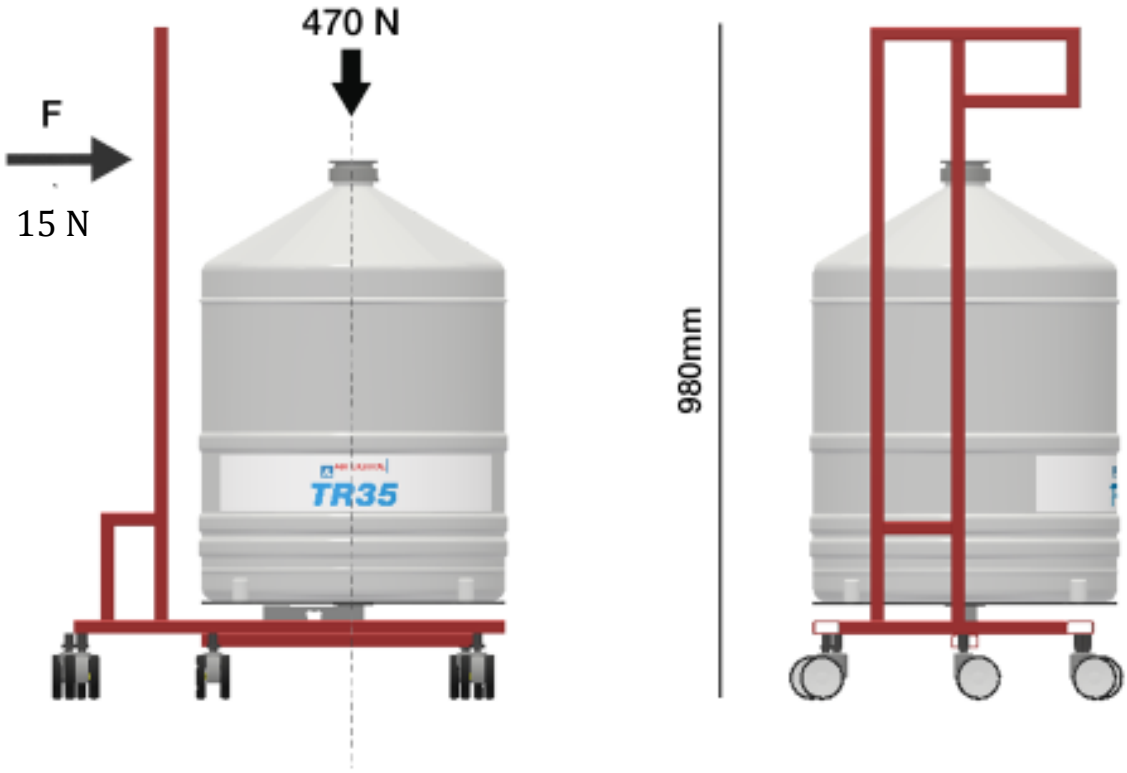


Figure 23 Upper framework design analysis

A castor wheel was selected for the framework with a larger radius of 32.5mm and a hard-polyurethane tread with an A87 shore hardness to reduce the rolling resistance.

The rolling resistance can be expressed as:

$$F_{rr} = \frac{C_{rr}\ W}{r}$$

Where:

- F_{rr} = Force of rolling resistance
- C_{rr} = Rolling resistance coefficient mm (0.77 for a polyurethane wheel material)
- W = Mass of the body in kg multiplied by (g) the acceleration of gravity $9.8\frac{m}{s^2}$
- r = Radius of the wheel in mm

An additional mass to 17kg was applied to the 47.95kg load acting in the same direction for the framework material weight and future mounted accessories, totalling, 64.95kg converting to Newtons = $64.95\ \times 9.8\frac{m}{s^2}$ = 636.5 N

Therefore, the rolling resistance (F_{rr}) of the framework can be calculated as:

$$\frac{0.77 \times \left(64.95\ \times 9.8\ \frac{m}{s^2}\right)}{32.5} = 15\ N$$

Thus, a force of 15 N is necessary to overcome the rolling resistance in a linear motion on a flat surface with the specified wheels.

Finally, the force required to accelerate the framework to a speed of $1.4\frac{m}{s}$ along a linear axis in 4 seconds was calculated, 4 seconds was specified as a steady acceleration to average walking speed, considering the safe handling of Liquid Nitrogen vessels.

The following formula was applied to find the acceleration: $a = \frac{(v_{f-}\ v_i\ )}{\Delta t}$

Where:

- a = acceleration
- $v_{f\ and}\ v_i$ = respectively the initial and final velocities in $\frac{m}{s}$
- Δt = the acceleration time

Therefore, the acceleration can be calculated as:

$$a = \frac{(1.4 - 0)}{4} = 0.35\ m/s^2$$

Rearranging the equation $F = ma$ to solve for F where:

- F = Force
- m = mass in kg
- a = acceleration in m/s^2

The following equation $a = \frac{F}{m}$ was used to find the net force in Newtons to accelerate the framework to a velocity of 1.4 metres per second (average walking speed).

$$0.35 = \frac{F}{64.95} \ \therefore \ 0.35 \times 64.95 = F \ \therefore \ F = 22.73\ N$$

The force $F = 22.73\ N$ was thus used to analyse the framework for displacement and safety factor in computational finite element analysis.

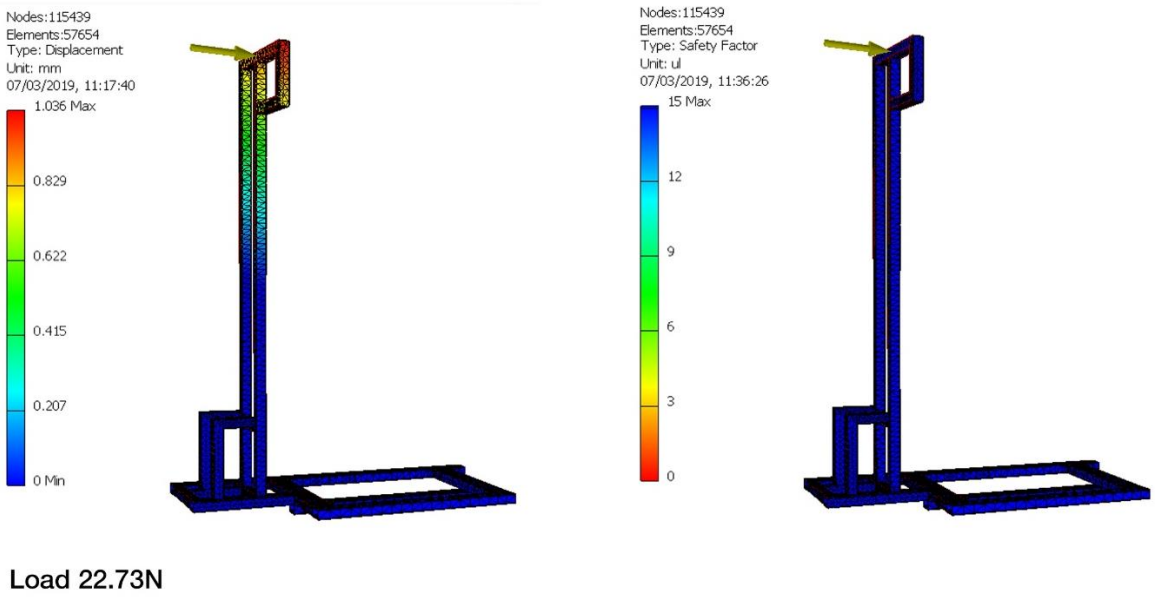


Figure 24 Framework stress analysis

Figure 24 above shows a negligible displacement of 1mm under acceleration force loading, subsequently dropping once travelling at a speed of 1.4 m/s. The analysis also shows a safety factor of 15, indicating the framework to withstand larger forces at the point of application, validating the material selection and profile.

Following the framework analysis, a basic loadcell and load plate assembly was modelled from the dimensions of the Liquid nitrogen Dewar and selected Mavin 100kg rated NA2 loadcell.

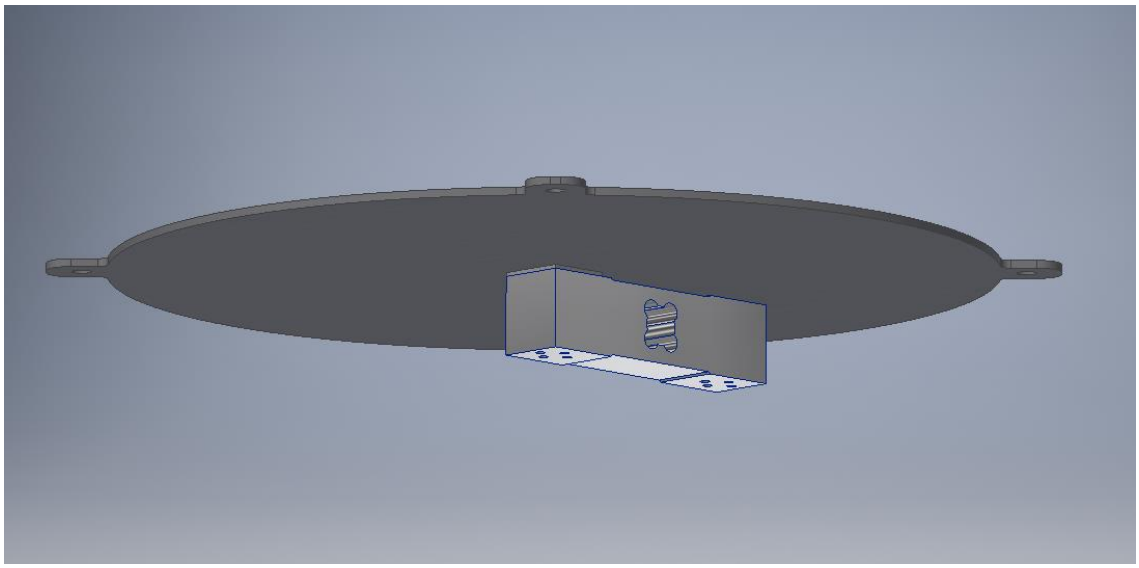


Figure 25 Load plate and loadcell standard assembly

The assembly was analysed using computational finite element analysis reviewing stress and safety factor under maximum operating load, to optimise the assembly for load distribution across the point of measurement; aiming to improve load measuring accuracy and prevent potential damage by distributing high stress points across the plate, and, designed to a safety factor of 3 for load bearing function.

The test loading parameters were kept consistent with previous analysis at 470 N with the load distributed through 5 points across the pressure plate using a refined mesh for accuracy.

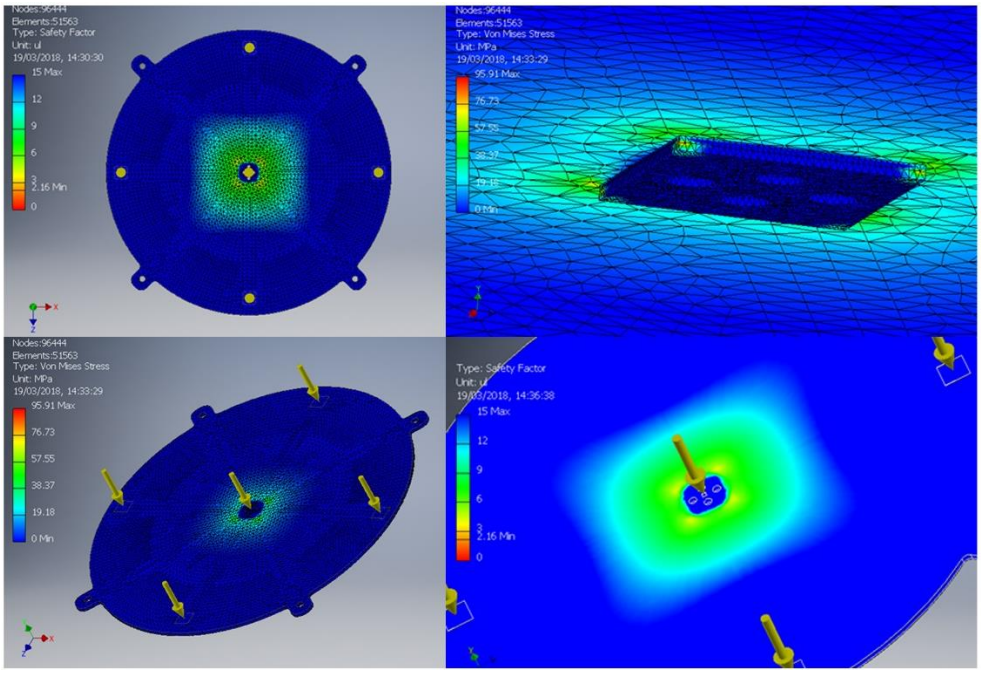


Figure 26 Load plate analysis

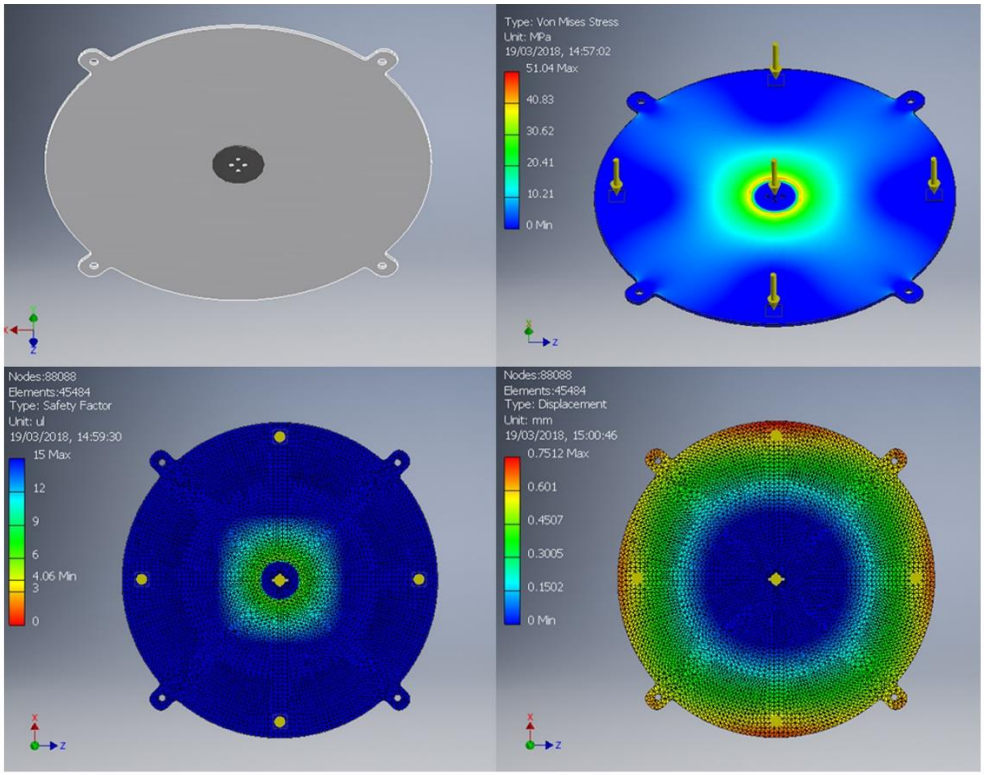


Figure 27 Load plate development analysis

A high stress was observed corresponding to the geometry of the square loadcell spacer shown in figure 26, leading to potential damage to the loadcell or load plate under improper loading conditions.

A cirular oversized Steel spacer was therfere designed to distribute the load, dissipating stress across the loading plate, figure 27.

Metric	**Edged Spacer**	**Circular Spacer**
VMS MAX	95.91 MPa	50.04 MPa
Safety factor MIN	2.16	4.06

Table 5 Comparative loadcell spacer analysis

The results in the table above show improvement in the performance of the assembly with a significant reduction in stress points and increased safety factor.

With a suitable base for further optimisation established the Loadcell pressure plate was optimised for weight to a safety factor of 3 (SF 3). This safety factor was determined considering load stability for accurate loadcell measurement.

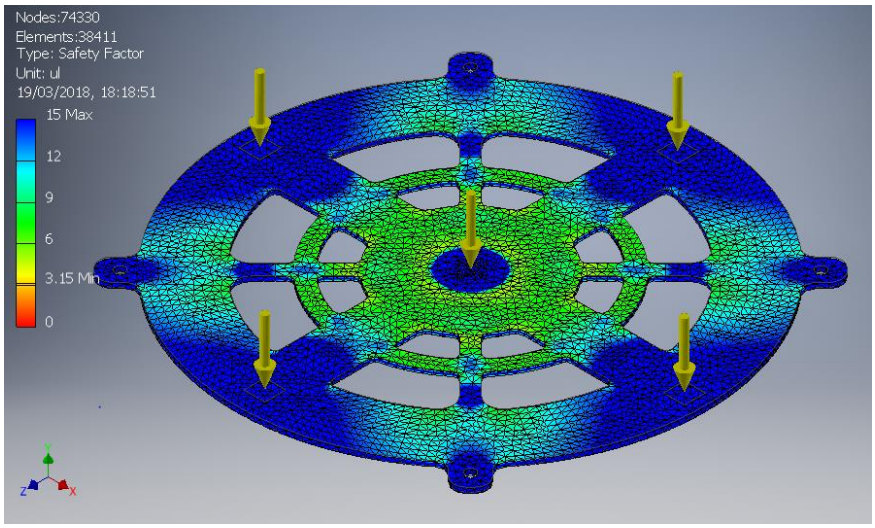


Figure 28 Optimised Load Plate design FEA testing

	Standard Plate	Optimised Plate
Mass (kg)	5.090kg	3.936kg

Table 6 Optimised plate comparison

The table above compares the component masses using the density of mild steel. A reduction of 1.154kg or 22.7% was achieved whilst keeping the safety factor to the specified SF3.

A mounting plate was designed for hardware to be mounted to the framework. A design for the mounting plate was explored to allow alternate hardware to be mounted in prototyping.

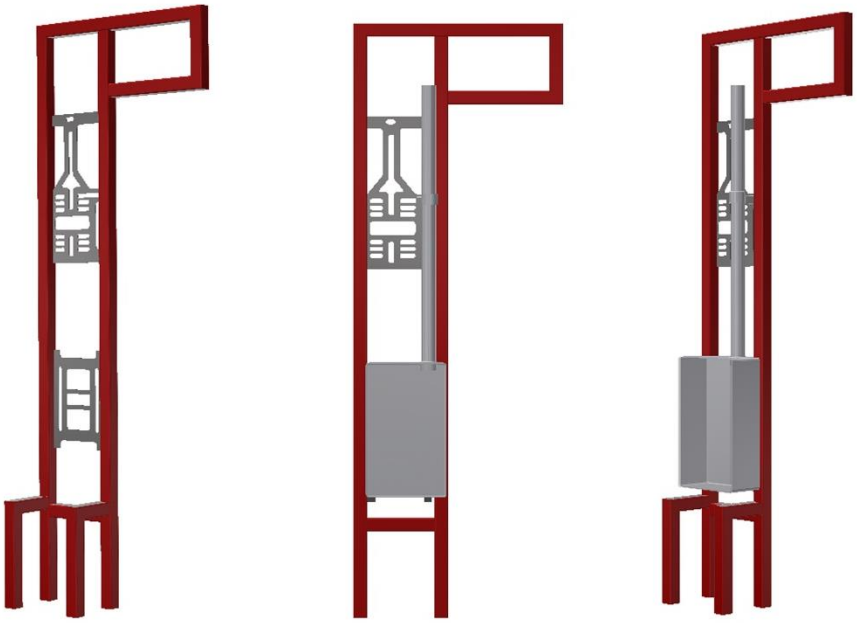


Figure 29 Framework mounting plates

Figure 29 above illustrates the mounting of the Electronics / Electrical Stimulation housing and cable routing conduit to the mounting plate. Additionally figure 29 shows the working envelope for the heating system and potential mounting configurations.

Figure 30 Framework Assembled

A prototype framework was fabricated, with steel welded and coated in a red oxide protective layer before being sealed with a hard enamel shell to protecting against humidity corrosion and aid cleaning.

The framework and loadcell assembly were tested with a load of 735 N both static and in motion, with no observed deformation in the framework or plate.

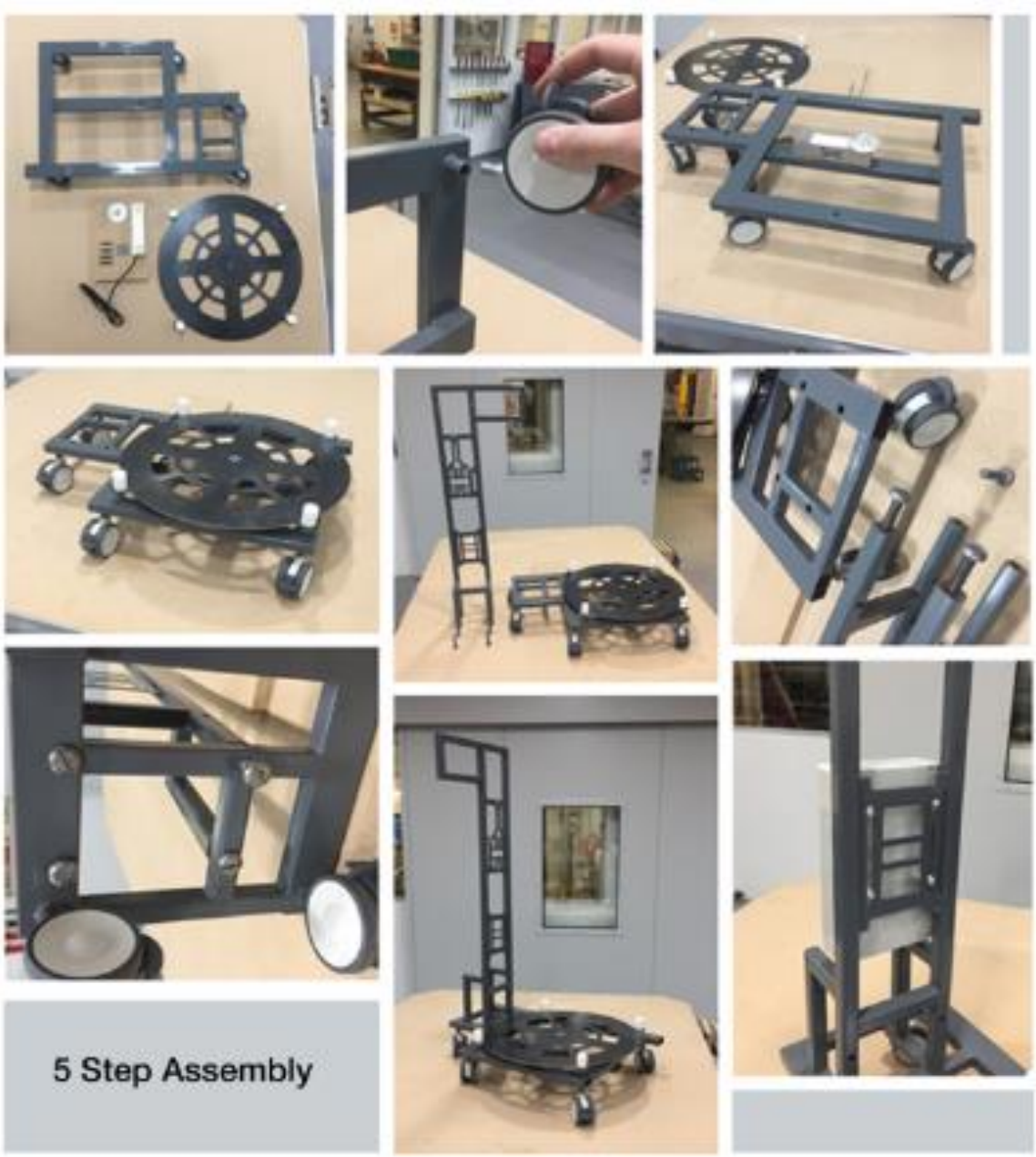


Figure 31 Framework step assembly

The figure above shows the step by step assembly process for the frame; broken down into 5 stages: fitting the castors to the threaded wheel positions, mounting the loadcell and spacer assembly, fitting the pressure plate, mounting and fastening the lower framework to the upright framework and filly fitting instrument housings.

The design allows for the assembly to be broken down for shipping / storage.

3.1.2.1 Prototype Heater Assembly

A heating system was designed to apply local heat without skin surface contact. After an initial review a prototype system with a working principal similar to a hair dryer was discussed with the client to explore the local application of heat with variable airflows, at different temperatures settings.

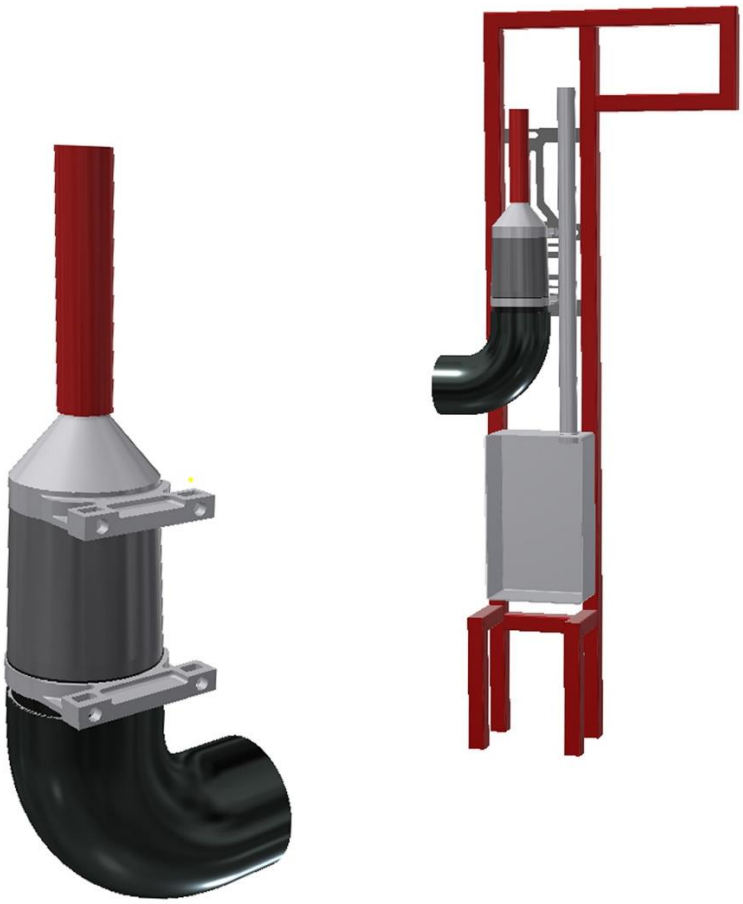
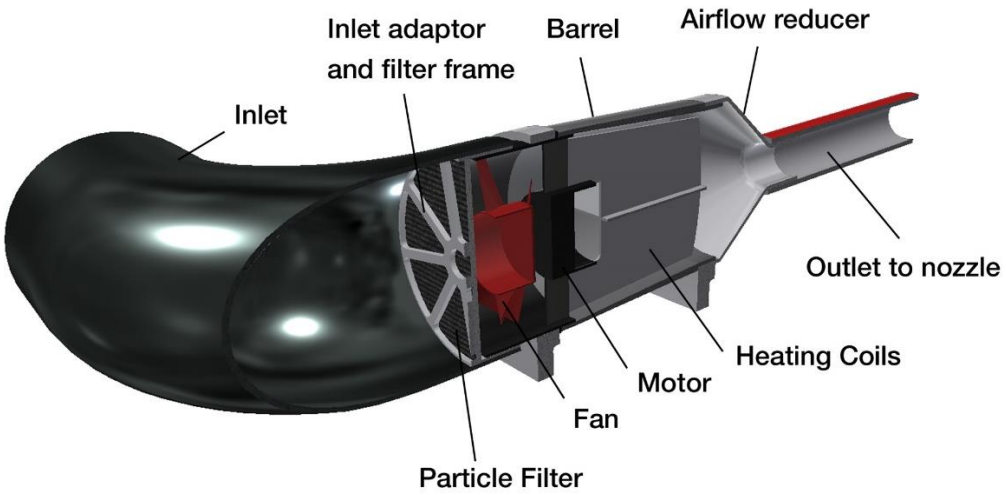


Figure 32 Heater Assembly overview

The system was designed simultaneously with the upright framework assembly to develop a compact configuration with a target output temperature of 40°C.

A modular prototyping methodology was adopted to allow iterative development, coupling rapid prototyping with analysis tools to optimise performance.

The figure below provides a half section overview of the prototype heating system and core components.



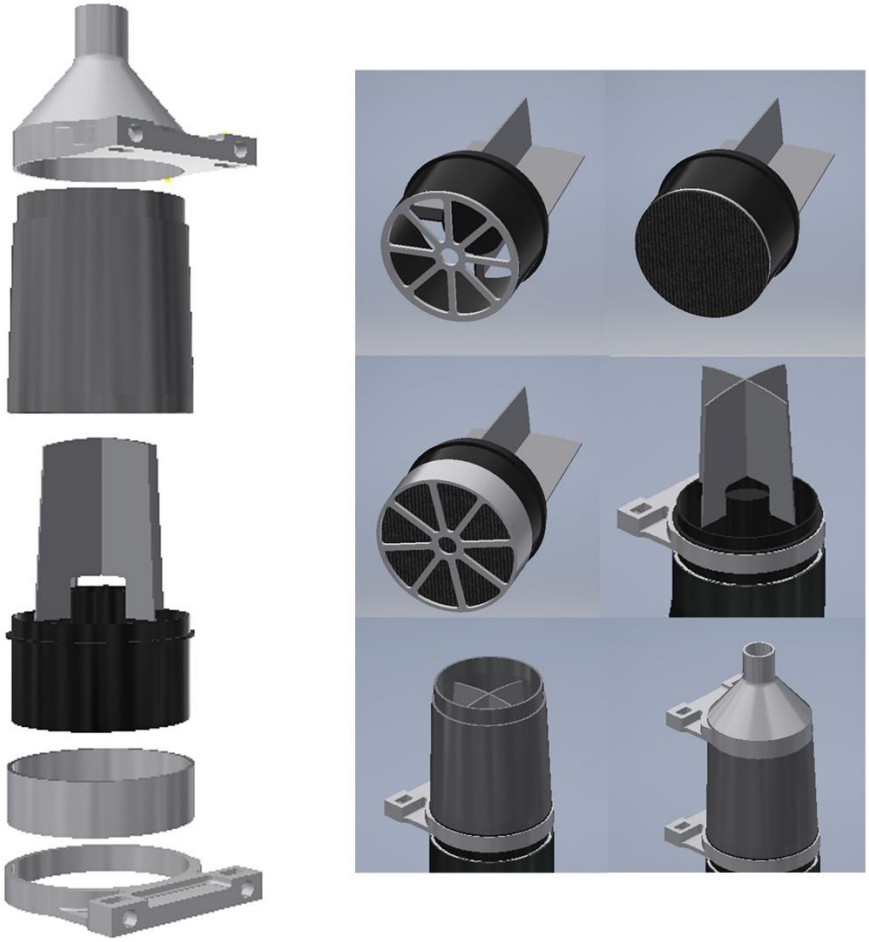


Figure 33 Heating system assembly

Figure 33 further details the system modularity. The assembly can be adapted to heaters with different properties; however, foremost enables rapid changing of the outlet flow reducer; allowing different profiles to be explored in development, with an aim to optimise airflow.

Figure 34 Airflow reading heater system

An initial analysis was performed with an airflow reading of 10 m/s average on a low speed pre-set heater setting.

The reading was taken using a Sealey TA070 Anemometer with built-in digital thermometer. An average temperature of 37.6°C over 30 seconds was recorded.

Using the equation of continuity shown below the initial readings were used to calculate a basic output velocity; considering air as incompressible; where V is velocity in m/s and A is area in m^2 with r being the radius from which area was calculated in mm.

$$V_{in} A_{in} = V_{out} A_{out}$$

or

$$V_{out} = V_{in} A_{in} / A_{out}$$

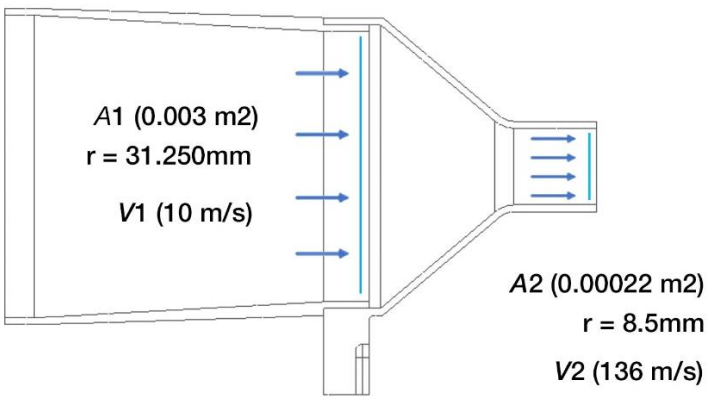


Figure 35 Heater flow continuity

A high outlet velocity of 136 m/s was calculated, indicating a potentially turbulent flow in the reducer design, suggesting a reduction in input velocity or an enlargement of the output area necessary to improve flow.

Computational Fluid Dynamics simulations were performed using Autodesk CFD 2018 to better understand the behaviour of flow and inform design solutions.

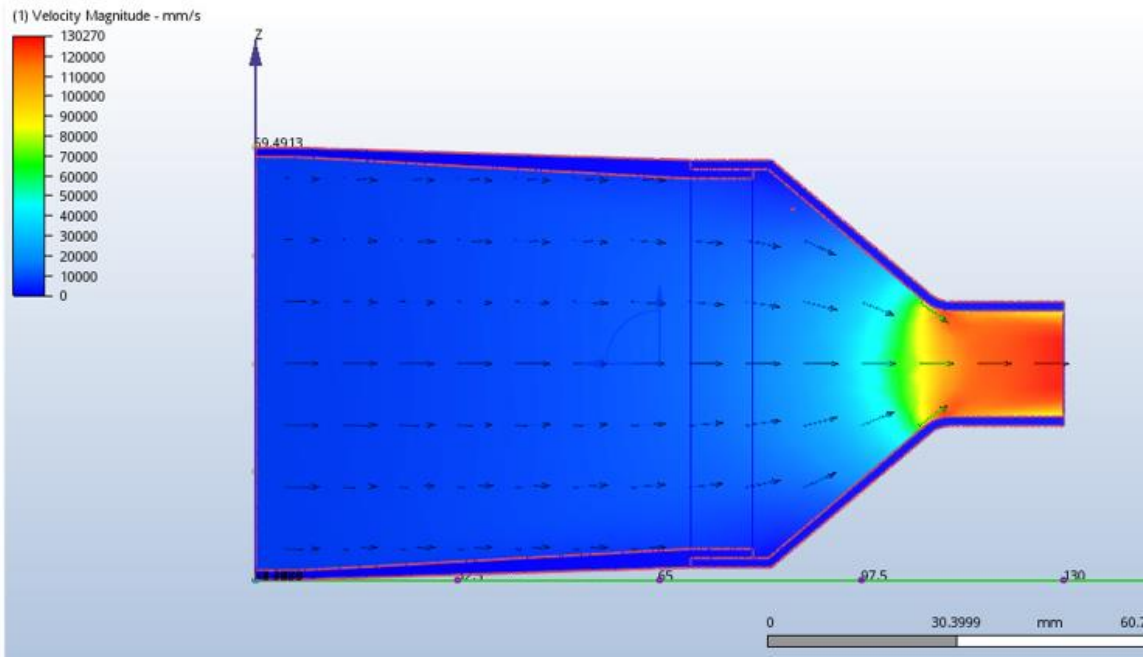


Figure 36 CFD Heater analysis

The analysis validated earlier calculations falling within 5% of the initial result with a simulated outlet velocity of 136 m/s.

Turbulence and static pressure were further analysed in the reduction profile to develop a more efficient reducer.

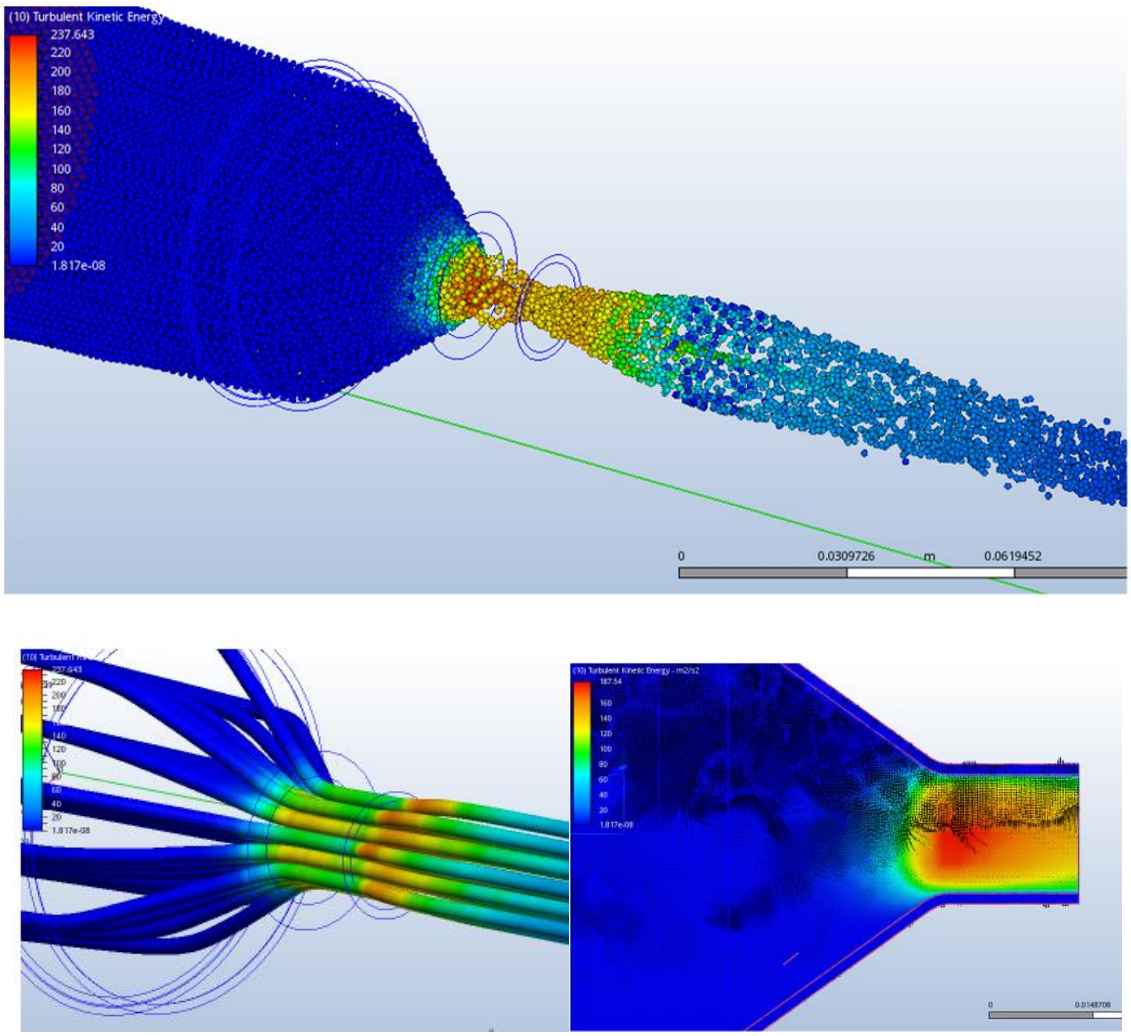


Figure 37 Turbulence model heater outlet

A turbulent kinetic energy of 187.54 m2/s2 was observed, highlighting a high amount of turbulent energy being extracted from mean flow at the nozzle. Figure 37 above taken from the turbulent kinetic energy simulation analysis visualises the results.

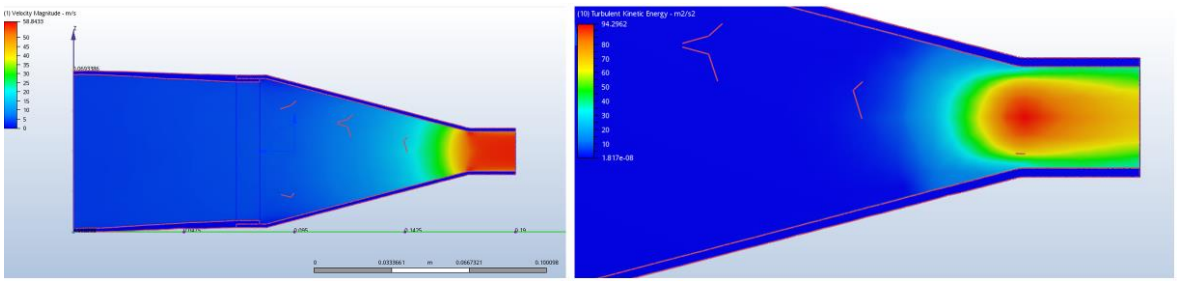


Figure 38 Alternate Nozzle profiles

Different nozzle profiles were explored and the inlet velocity set to 5 m/s to reduce turbulent flow through the system. Figure 38 shows a longer reduction profile resulting in a reduced TKE (turbulent kinetic energy) of 94.2 m2/s2.

Through research an eccentric reducing profile was developed to facilitate proper transition from the larger diameter outlet to the nozzle.

Figure 39 Eccentric reducer design

CFD analysis was performed on the eccentric reducer with an inlet velocity of 5 m/s and a density relative to air at 60°C defining the mass flow rate. The simulation showed a significant reduction in the TKE at 64.7 m2/s2 and velocity magnitude of 58.9 m/s.

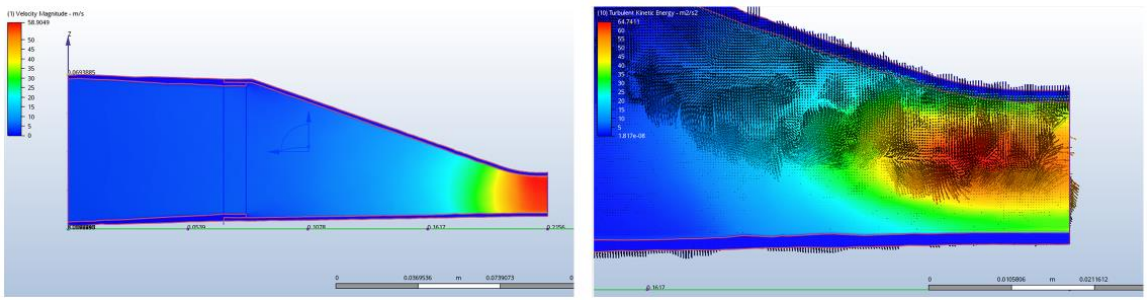


Figure 40 Velocity and TKE eccentric reducer

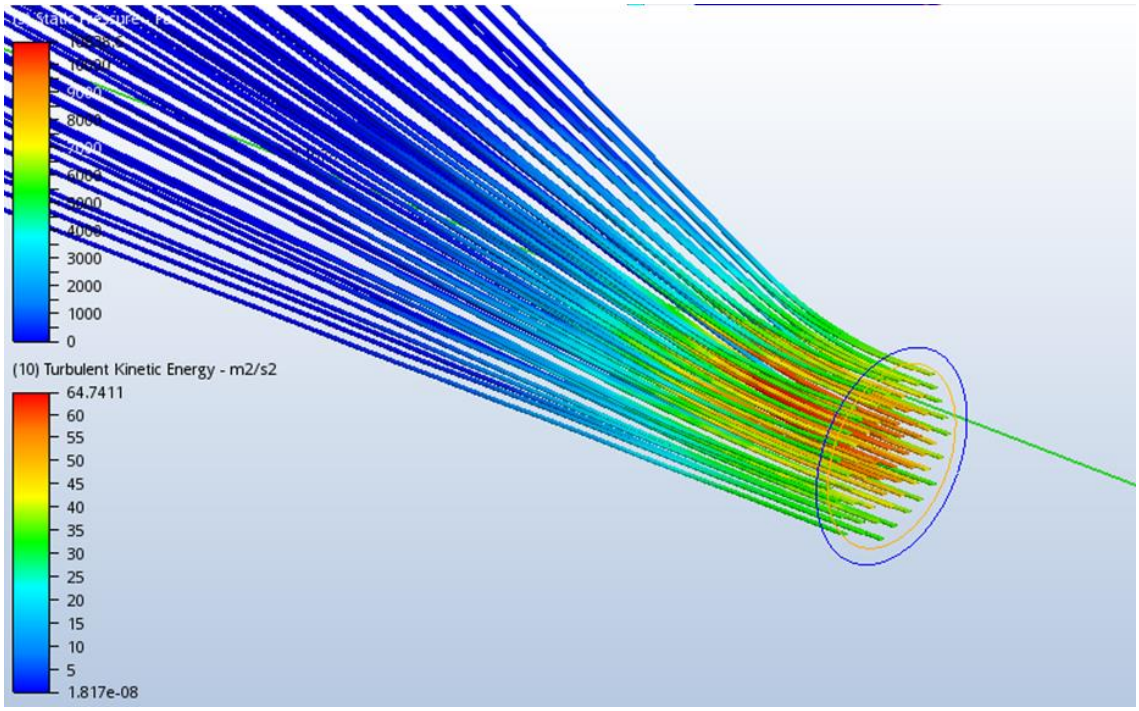


Figure 41 TKE Particle flow eccentric pipe

Further simulations were performed to comparatively analyse the original reduction profile and the eccentric design considering a 1m application pipe attached to the nozzle.

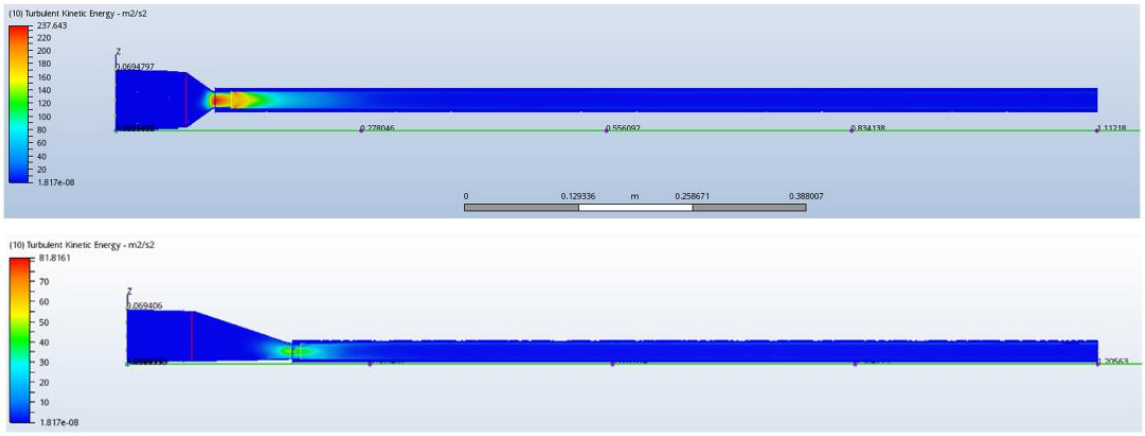


Figure 42 TKE Flow comparison eccentric vs concentric

The comparison shows an improved TKE value in the eccentric reducer design with attached pipe. Therefore, suggesting a less turbulent flow through the system and better flow quality.

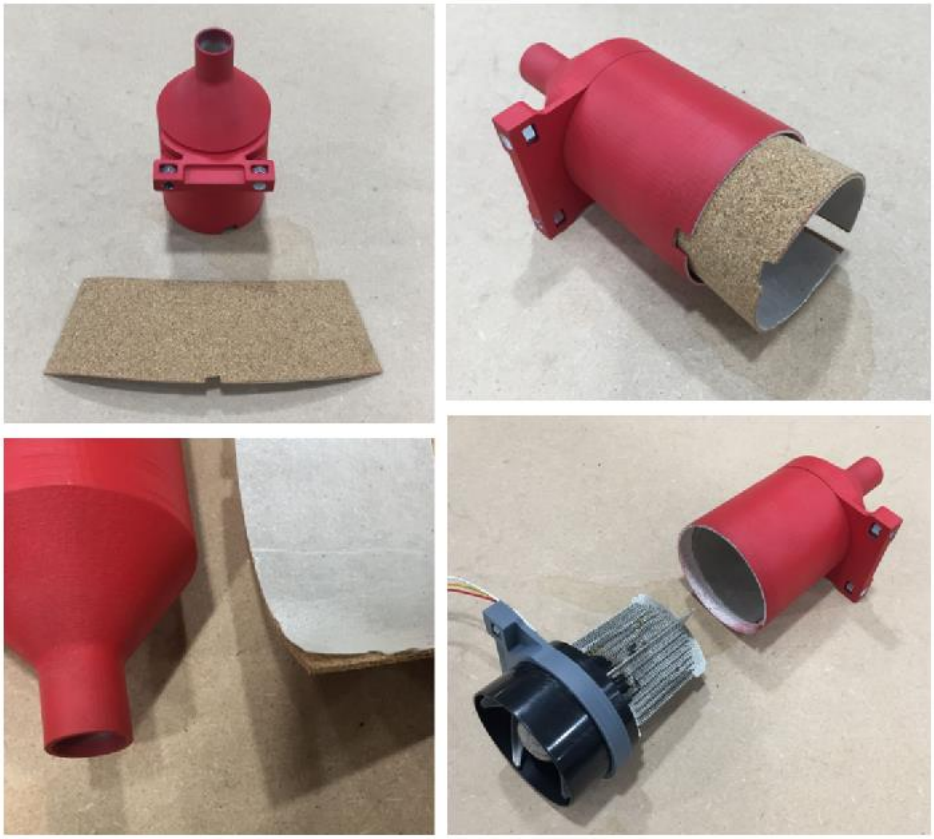


Figure 43 Heater system prototyping

A prototype was 3D printed and insulated with a cork backed sheet silicate (phyllosilicate) mineral insulator for intense heat applications to allow testing.

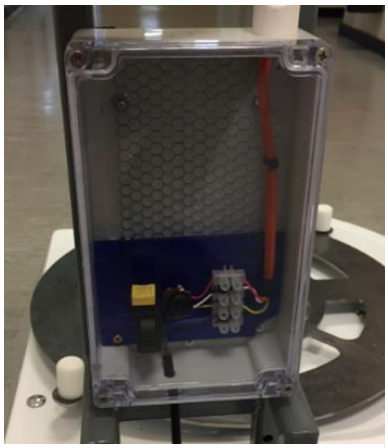


Figure 44 Heating system control

The control circuit was mounted and isolated within the electronics enclosure. From here the settings for temperature and fan speed can be controlled to calibrate the system.

A handle and holder were designed to meet the ergonomic requirements of the application, with a focus on user comfort and practicability.

Figure 45 Heater Handle and holder

Considering the repeat pick up/put down process observed in the ethnographic study, the handle was designed for rapid mounting/dismount from the holder. Further innovations in the design experiment with channelling airflow through the holder itself, as shown in figure 46 below. The component shows the potential application of 3D printing as a manufacturing process, allowing geometries otherwise difficult to produce in small quantities to be made efficiently and at low cost.

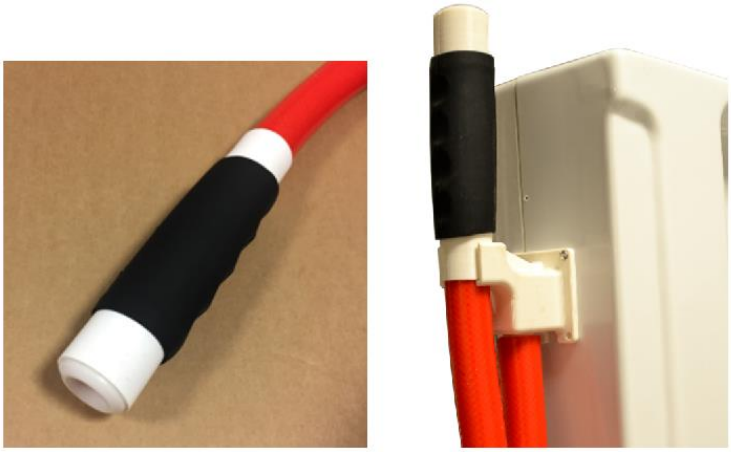


Figure 46 Heater handle and holder prototype

Figure 47 Further heater testing - Temperature

The system was mounted to the framework and further tests performed with varying inlet velocities. An inlet velocity reduced to 5 m/s is shown in figure 47 above, with an outlet velocity reading of 15.2 m/s at a temperature of 60.2°C.

From the tests it was concluded that further work would be required to deliver a stable airflow. The system was observed to achieve an outlet flow temperature of 40°C and above, however pressure drop in the system was also observed when attaching a pipe of 20mm internal diameter and 1m in length, resulting in poor flow. Areas for investigation include: Further reducer design and calibrating the fan speed to improve flow quality, alternatively considering different modes of heating.

3.1.2.2 Electrical Stimulation Unit

An electronic stimulation unit meeting the technical specifications for variable procedures outlined in the literature review was selected for prototype development.

Figure 48 Electrical Stimulation unit hardware

The unit features a multiple channel output, with a 30-260 us pulse width and 2-150 HZ pulse rate. Particular attention was given to quality in selection, with the unit being CE marked and fully compliant to the medical derivative class 2A.

The unit was mounted to the electronics enclosure and tested with different settings. From the enclosure the procedure parameters can be manually configured, and the device turned on and off.

Figure 49 EMS handle mount

Again, considering user ergonomics a rapid probe mounting system was designed with a plug-in interface for switching between probes and other pads, shown above.

The design features a custom probe handle, figure 50, allowing for research into different probe materials.

The handheld probes were designed considering ergonomics in their form and simplicity in function. With further development an interchangeable head system could be designed to allow variable probe sizes for different procedures.

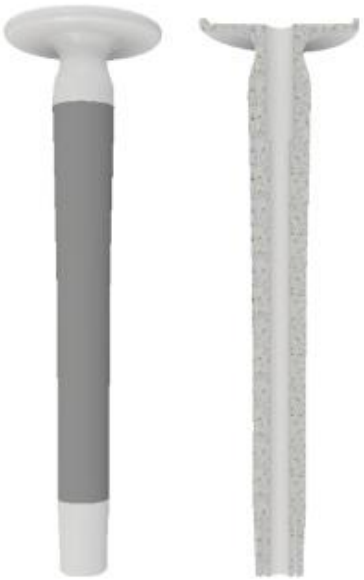


Figure 50 EMS Probe design

Figure 51 EMS/Heater electronics

The electronic stimulation unit was isolated from moisture within the IP65 rated electronics housing alongside the heater control circuit.

Steps for further development include the design of a microcontroller circuit board to control the Heating application, EMS and Liquid Nitrogen pump/sensors from a Graphic User Interface GUI.

3.1.3 Bodywork and Interface design and development

Developing on earlier card and foam model studies a prototype bodywork was designed exploring form, aesthetic and suitability for low volume manufacture.

Figure 52 Bodywork CAD surface modelling

The design aimed to communicate a medical language whilst addressing the challenges presented by the clinical environment, particularly the sterilisation of surfaces and space efficiency. To address this a concept was developed minimising the surface area of the bodywork and avoiding hidden hard to reach surfaces.

The figure on the following page, figure 53, details early findings from an ergonomic design assessment. It was observed that design features such as removing obstructive geometries by rounding corners could improve ergonomics when interacting with and working around the machine.

Figure 53 Ergonomics in the working environment, cutting the corners.

Feedback from ergonomic model studies and observations were translated into a digital model from which a physical high detail scale surface model was produced.

Figure 54 High detail finished foam surface model

The model was machined in components on a CNC router and assembled/finished by hand. The soft modelling process allowed an understanding of how the components break down into moulds, along with an assessment of the most appropriate methods of manufacture for the prototype and going further in larger production volumes.

Considering the geometry and dimensions Vacuum forming was identified as an appropriate low cost, rapid manufacturing process.

A set of tools were designed to meet the requirements of the vacuum forming process, considering draft angle, ventilation and surface quality.

Figure 55 Vacuum forming mould tools

The tools were fabricated from scrap offcuts of MDF and machined on a flatbed gantry CNC router. Toolpaths were designed and optimised for MDF cutting, significantly reducing the time and cost to manufacture the tools. Finally a high quality mould paint was applied and the tools prepared to a smooth surface finish for vacuum forming surface quality.

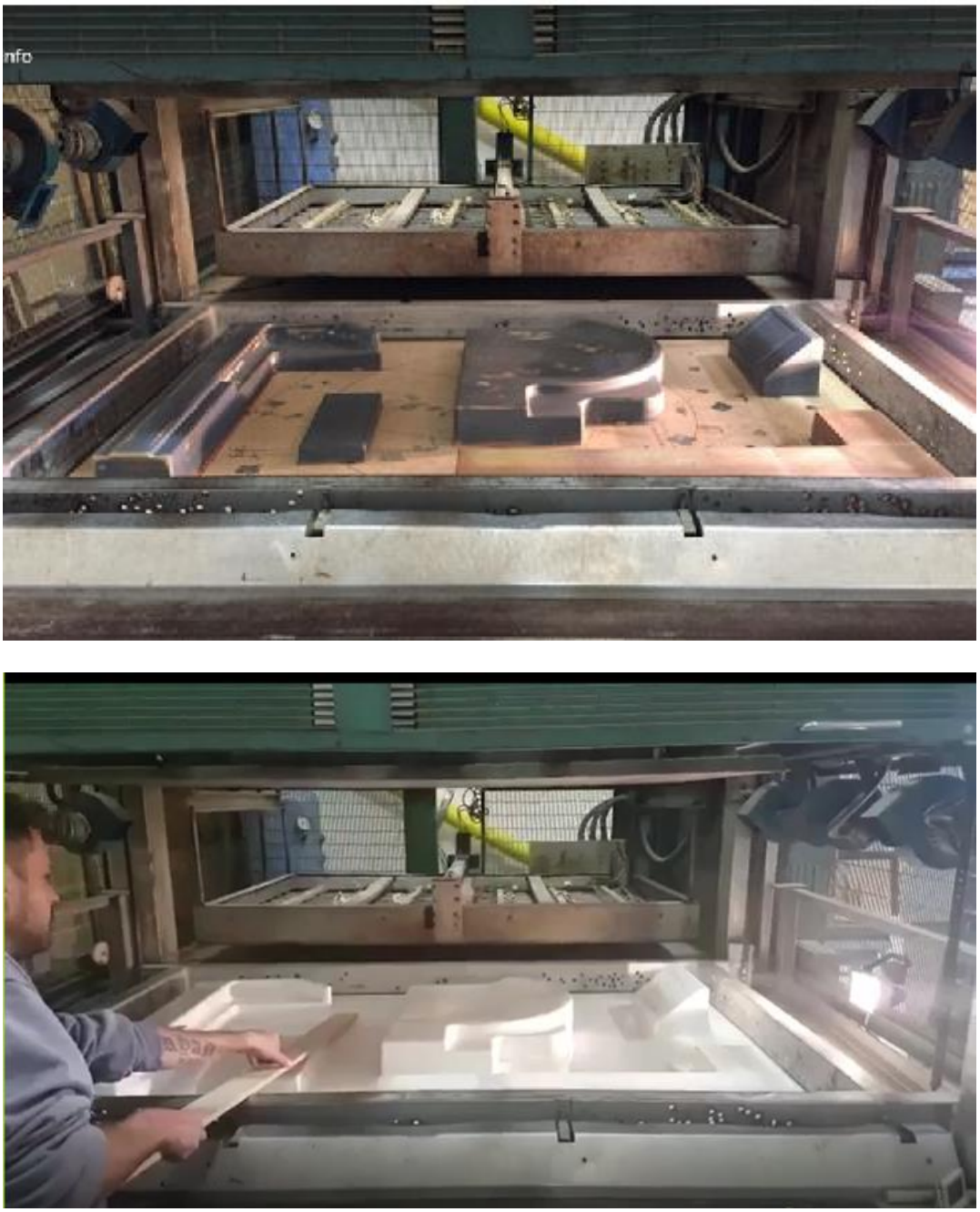


Figure 56 Large format vacuum forming set up and HIPS moulding

The mould tools were shipped to a Vacuum forming facility with a large format vacuum forming machine able to produce a complete set of formings from a single draw/sheet of material, reducing the manufacturing time and cost.

3mm High Impact Polystyrene was selected for the prototype with material properties including high impact resistance, FDA compliant, high quality finish and low cost.

The formings were post processed to the required dimensions and adapted for assembly with components test fitted and evaluated.
Figure 57 shows the screen test fitting and commissioning.

Figure 57 Screen test fitting

Following this the prototype was fully assembled, and the overall integrity of the structure assessed with a focus on build quality, aesthetics and functionality.

Figure 58 Fully assembled machine overview

Figure 59 Prototype bodywork Photographs

The figure above presents multiple views of the assembled machine with EMS plug in panel and probes mounted, screen affixed and the heater holder in place. Following a review of the overall assembly and presentation to the client, positive feedback was received on the design.

3.1.4 Liquid Nitrogen Vapour Pump and accessories

It was realised during the course of the research that a Liquid Nitrogen Vapour pump system including pump and hose suitable for the project was not accessible within the budget. The issue was presented in a project meeting to supervisors and the feasibility of developing a pump in house was discussed.

Following research into to existing products and literature on the topic of Liquid Nitrogen vaporisation a design was proposed based on a method described in a paper titled, Latent Heat of Vaporisation of Liquid Nitrogen (Lucas, 2010)

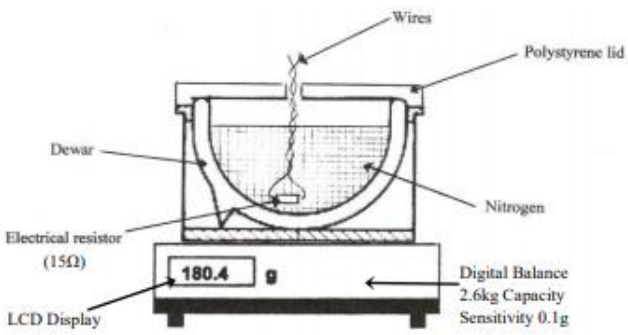


Figure 1: Schematic diagram showing latent heat of Nitrogen measurement apparatus [2].

Figure 60 presents a schematic for the method using a resistor submerged in Liquid Nitrogen resulting in heat energy transfer between the electrical heater and surroundings and the LN2.

Figure 60 Method of LN2 Vaporisation, Lucas 2010

The method detailed above was found to be used in current products on the cryotherapy market to produce a jet of refrigerated Nitrogen vapour, including localised cryotherapy market leader Metrum Cryoflex.

With further investigation a patent published by Metrum Cryoflex was found protecting a similar invention in Poland, therefore measures were taken to avoid infringement in design.

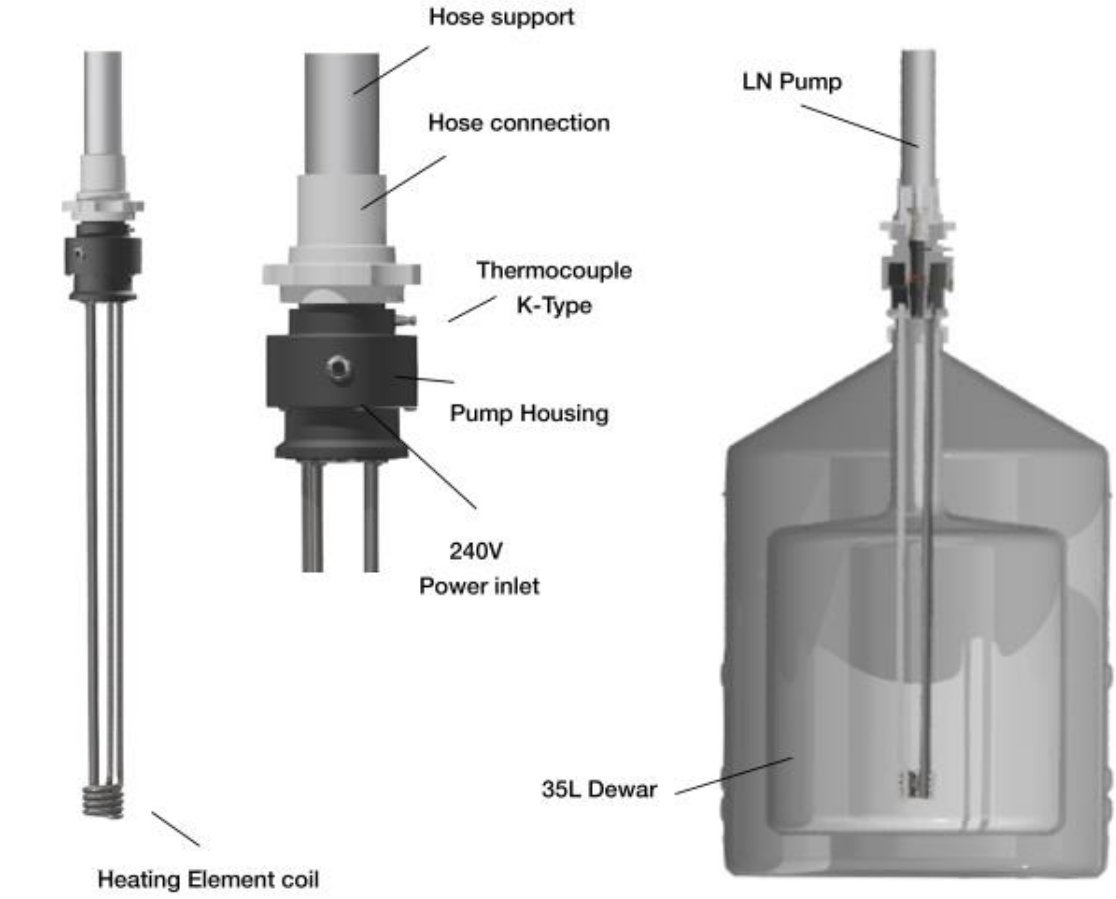


Figure 61 Pump design schematic parts label

The figure above details the LN2 pump assembly designed at London South Bank University.

The design produces a jet of refrigerated Nitrogen vapour by applying electrical current to a heating element submerged in a dewar of Liquid Nitrogen (LN_2). Electrical resistance in the coil of the element produces heat, resulting in heat transfer to the surrounding LN_2. The heat energy changes the Liquid Nitrogen state to Nitrogen gas with the temperature remaining constant.

As the expansion ratio of LN2 changing state to Nitrogen is 1:694 a pressure build up in the Dewar vessel produces a pressurised jet of refrigerated Nitrogen Gas at the outlet; channelled through the pump housing, hose and handle through to the nozzle.

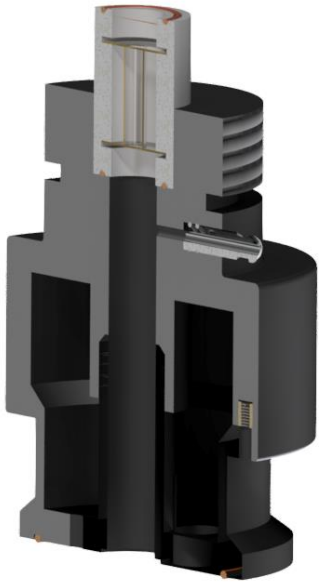


Figure 62 shows a cross section of the pump housing with a 15mm diameter Nitrogen Vapour channel. Research into materials for cryogenic applications identified Carbon filled PTFE as appropriate for the pump housing; offering a higher dimensional stability at cryogenic temperature than virgin PTFE and offering good electrical properties whilst being an FDA approved material.

Figure 62 Cross section pump housing

The design uses o-rings to seal the housing preventing vapour leakage; tolerances were designed into o-ring mating surfaces to BS ISO 3601 specification. A fluid pressure test can be performed on the assembly to ensure the pump housing can withstand working pressures.

The pump further features an integrated K-Type thermocouple to measure the temperature of the Nitrogen Jet, allowing digital temperature readings at the pump head to be displayed and monitored.

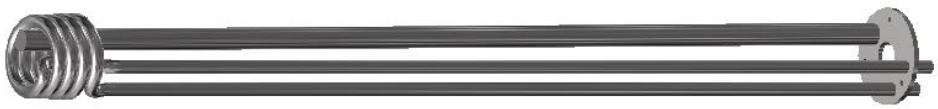


Figure 63 Heating element coil design

A 1000-watt 240V heating element was designed for the Air Liquide TR35 dewar vessel. Specifications were supplied to an element manufacturer for the fabrication of a prototype element in stainless steel 304, a material widely used in Cryogenic applications.

Figure 64 Mounted Pump Liquid Nitrogen Dewar

The element features a 47mm max diameter 4 turn coil with an 8mm pitch and -2.0° coil taper.

The element is designed with an active hot section up to 55mm from the base of the coil, allowing only the element coil to generate heat to improve efficiency. A minimum operating level of 7.3L is required to keep the coil submerged to prevent dry heating and damage.

A space of 50mm was left between the dewar and coil further preventing heating and deforming / damaging the dewar vessel.

During the design process it was observed in existing products that particles or droplets of Liquid Nitrogen could be drawn through the vapour stream, presenting significant risk of cold injury to users including cold burns and frostbite.

A novel vapor filtering system was designed to improve the safety of the system, preventing particles from being drawn through the vapour stream and causing potential injury to users.

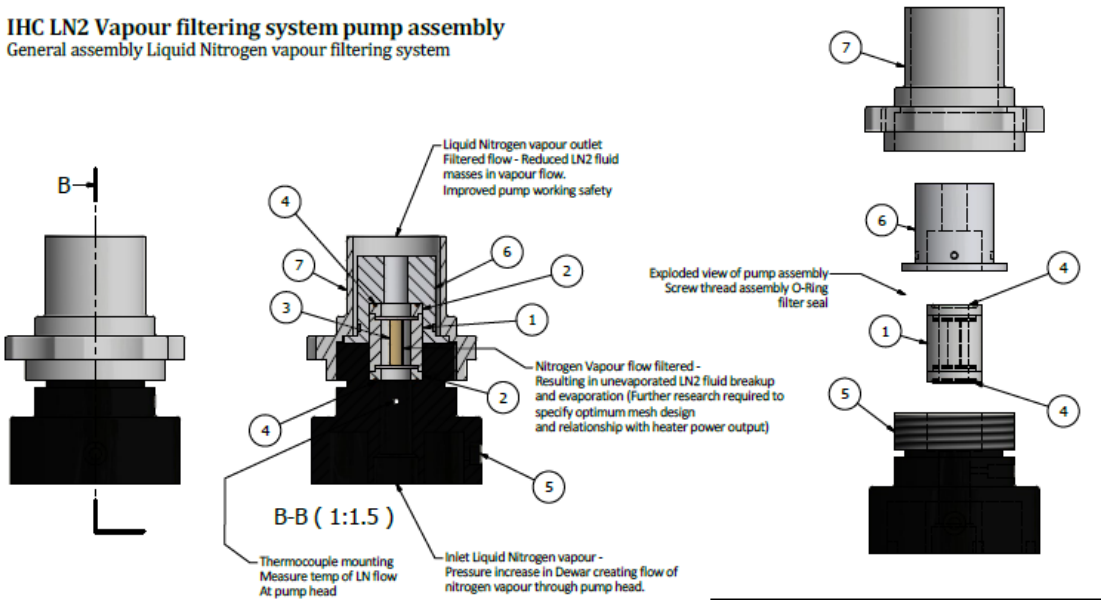


Figure 65 Liquid Nitrogen vapour filter design

The figure above details the general filtering pump assembly and components with further details of the design supplied in the technical drawings.

The Prototype was manufactured, assembled and evaluated.

Figure 66 Pump manufacture and assembly

Following assembly and commissioning the pump was tested with a 30V power supply at 0.5 amps, reaching a temperature of 67°C. An insulation resistance check was performed reading 3M ohms, indicating part of the PAT regulation to be met.

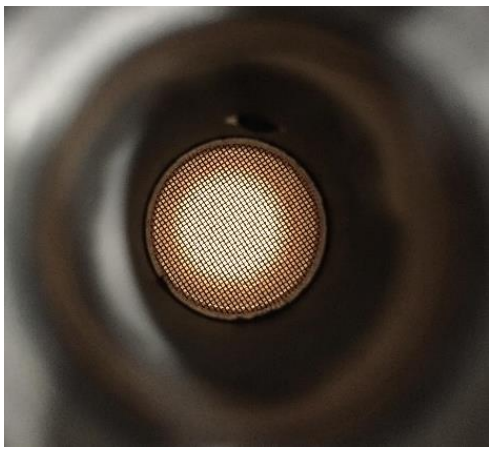


Figure 67 LN filter Mesh screen

The vapour filtration system was tested with pressurised air through the vapour channel for flow continuity. The test concluded the flow to not be significantly reduced by the filter, however a refinement to the mesh design could optimise the vapour filtering process, presenting opportunity for further research into optimising Liquid Nitrogen vapour Filtration.

Figure 68 Pump assembly Photographs

A testing plan composed of seal pressure test, electrical PAT test and LN2 vaporisation test was researched, using a variable voltage transformer to measure nitrogen vapour flowrates at different voltage settings up to 240v; establishing optimal procedure settings with estimated output jet temperatures of between -130°C to -170°C

Due to University health and safety policy and project time constraints further testing was considered outside of the projects scope, however, the vapour filtering pump design was explored for potential IP, with technical drawings and documents disclosing the innovation supplied to a patent lawyer on behalf of the client for review. attached in the document appendix.

3.1.4.1 Cryotherapy Handle and Flexible Hose

A handle was designed considering user ergonomics to apply the jet of refrigerated Nitrogen vapour to a target area. The design explored the incorporation of a temperature sensing module to measure live temperature across a target area.

Figure 69 Nitrogen Handle and Infrared thermometer

A DFRobot TN9 long distance infrared thermometer module was selected to measure surface temperatures between -33°C to 220°C for medical applications. The module allows high accuracy temperature reading without surface contact.

The module allows a feedback loop controlling the element temperature to be programmed; allowing the surface temperature readings to control the vapour flowrate, resulting in keeping the surface area at a constant pre-set temperature. Furthermore, the sensor enables a measure of safety, enabling automatic cut off as a measure to control risk; as outlined in BS 14971 – Application of risk management to medical devices.

A flexible 2m insulating hose was designed to channel refrigerated Nitrogen from pump to handle with minimal external heat transfer to the vapour stream in pipe.

Figure 70 Cryogenic pipe development

The hose was developed from a stainless steel 304 flexible hose with a 2mm PFTE lining, the hose was further insulated with a PFTE external wrap and an adhesive pipe insulation before being sealed with a flexible heat shrink. A 15mm internal diameter nozzle and threaded pump coupling profile was machined from 304 stainless steel. This early prototype allowed material flexibility performance to be tested, however with further development Fourier's equation for heat conduction could be used to optimise the insulation thickness for performance at room temperature.

3.1.5 System Architecture

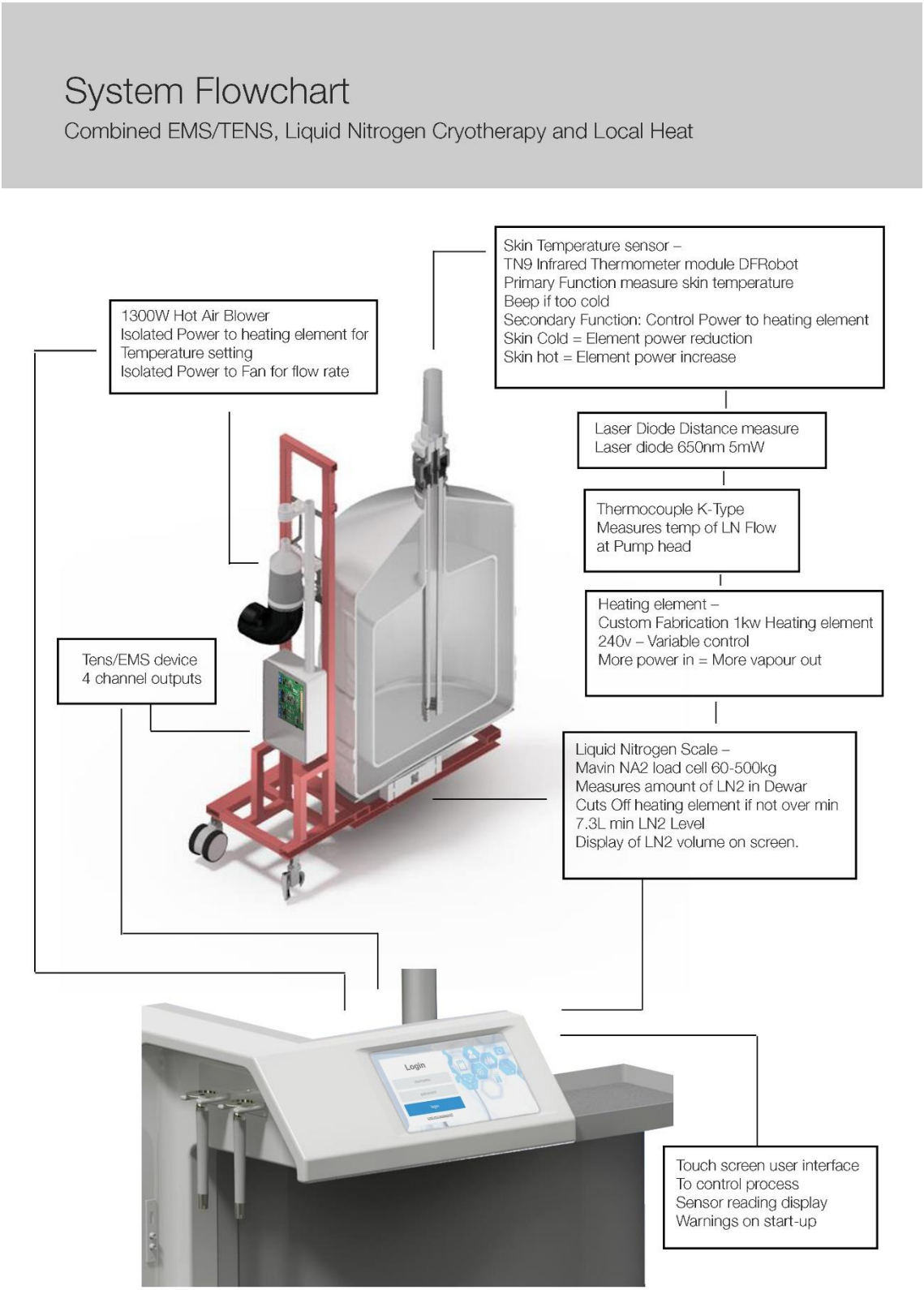


Figure 71 System architecture

3.1.6 Device warning signs

Further considering BS EN ISO 14971:2009 the Application of risk management to medical devices; appropriate warning labels communicating potential risks and measures to reduce risk were identified for placement on the device, product documentation and in the working environment.

Figure 72 Device warning signs

The figure above displays signs to feature on the product for user safety, to be located in areas with good visibility.

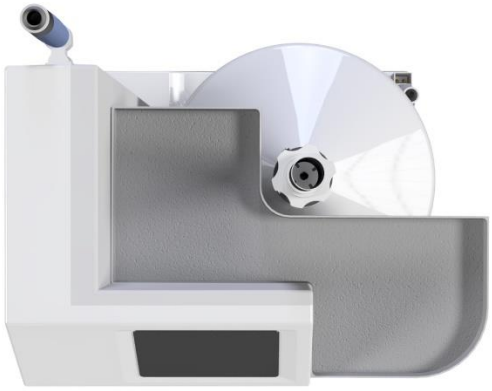
3.1.7 Product Information Booklet and Manual

Local LN2 Cryotherapy
EMS/TENS and Heat

Liquid Nitrogen vapour filtering Pump
Thermocouple temperature measure
Carbon Filled PTFE construction
Improved safety design

35L Liquid Nitrogen dewar
Loadcell quantity measurement

High manoeuvrability wheelbase
Frame designed to 150kg load capacity
Minimal footprint



Compact Footprint
Designed to free floor space around the machine

Ergonomically Designed
Designed for comfortable use in the working environment with improved functionality

Local LN2 Cryotherapy
EMS/TENS and Heat

User Manual

The device is a Liquid Nitrogen based cooling device reaching temperatures of -160°C at the application nozzle outlet. The device is designed for use in health and wellbeing clinics, rehabilitations centres and physiotherapy centres.

Environmental operating conditions:

- Temperature range: +10°C / +30°C
- Relative humidity range: 30% / 75%
- Atmospheric pressure range: 700hPa / 1060hPa

Transport conditions:

- The device has to be transported in a vertical position.
- Temperature range: -10°C / +45°C

WARNINGS

- Direct Contact with Liquid Nitrogen may cause burns. Details for safe handling are given in the material safety data sheet of Liquid Nitrogen.

- Danger of burns, when filling the tank with Liquid Nitrogen and in other instances which contact with skin might occur protective clothing must be worn, protective mask and gloves obligatory.

- Danger of burns, Liquid Nitrogen may flow through the nozzle in initial set up and first few minutes of device operation, when turning on the device after refilling you should:

Direct the nozzle at the floor
Set minimum cooling level

- The device has to be connected to a power supply of 230V.

- The device should only be operated by users trained in the use and operation of the device and safe handling of substances.

STARTING PROCEDURE

1. Place the Full Nitrogen Dewar in the centre of the load plate between the stoppers.
2. Insert vapour pump coil into the Dewar with caution.
3. Clamp pump to Liquid Nitrogen Dewar.
4. Connect the pump to machine pump power outlet.
5. Connect Thermocouple and infrared temperature module to device body plug-ins.
6. Connect 230V power cord to IEC filter panel.
7. Turn on and run test setting from user interface.

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London South Bank Uniiversity

MSc(Res) General Engineering 2018

Figure 73 Product information booklet and manual

4 Conclusions

This section concludes the report with a review of the project through its development, assessing the prototype delivery against key performance specification metrics, including scope and recommendations for further development with a view to manufacture.

The project successfully delivered on the initial brief; establishing a modular proof of principal prototype to facilitate further technical research and development in the application and efficacy of core independent and combined functions, including; a framework, heating system, electrical stimulation unit and Liquid Nitrogen vaporising pump.

This early work considered the challenges in bringing to market a combined unit, particularly focusing on conceptualisation of a working configuration to consider user interaction, ergonomics and machine functionality in the product environment.

Adopting a new product development methodology and structured development plan ensured the delivery of quality and consideration of standards throughout; however, the breadth of topics covered in the project and constraints, including time and funding, limited the research and development to a low iteration count; restricting the natural cycle of feedback driven iterative design and testing loops, therefore, limiting the potential for innovation and impact through research.

Addressing this, resources were allocated to areas with greater research impact potential, for instance, the Liquid Nitrogen vapour pump; resulting in innovative design and the generation of new IP. However, given the time constraint and project scale a larger development team would have been beneficial to simultaneously develop different

systems within a development framework, allowing rapid development and greater potential for the delivery of innovative products / solutions.

Going further, the design of a circuit board and control program including research into the development of a graphical user interface (GUI) would be necessary and more appropriately attributed to research in the fields of Electronic Engineering and software development to meet IEC-62304 standards for medical device software. Additionally, rigorous testing of the current prototype to standard would be required in bringing the product to market and the prototype subject to modification to meet regulation prior to manufacture.

Recommendations: Although an initial architecture and prototype for the device has been detailed for next phase development and manufacture, the market research and summary of published literature should be considered, with alternative methods of lower risk, lower cost and more commercially accessible combined cooling procedures explored.

However, in the case of project continuation a manufacturer working to relevant medical product standards should be approached for further testing and development. Additionally, alternative case uses for components, in particular the Liquid Nitrogen vapour pump should be reviewed for potential as a standalone product with applications in the applied sciences and Engineering.

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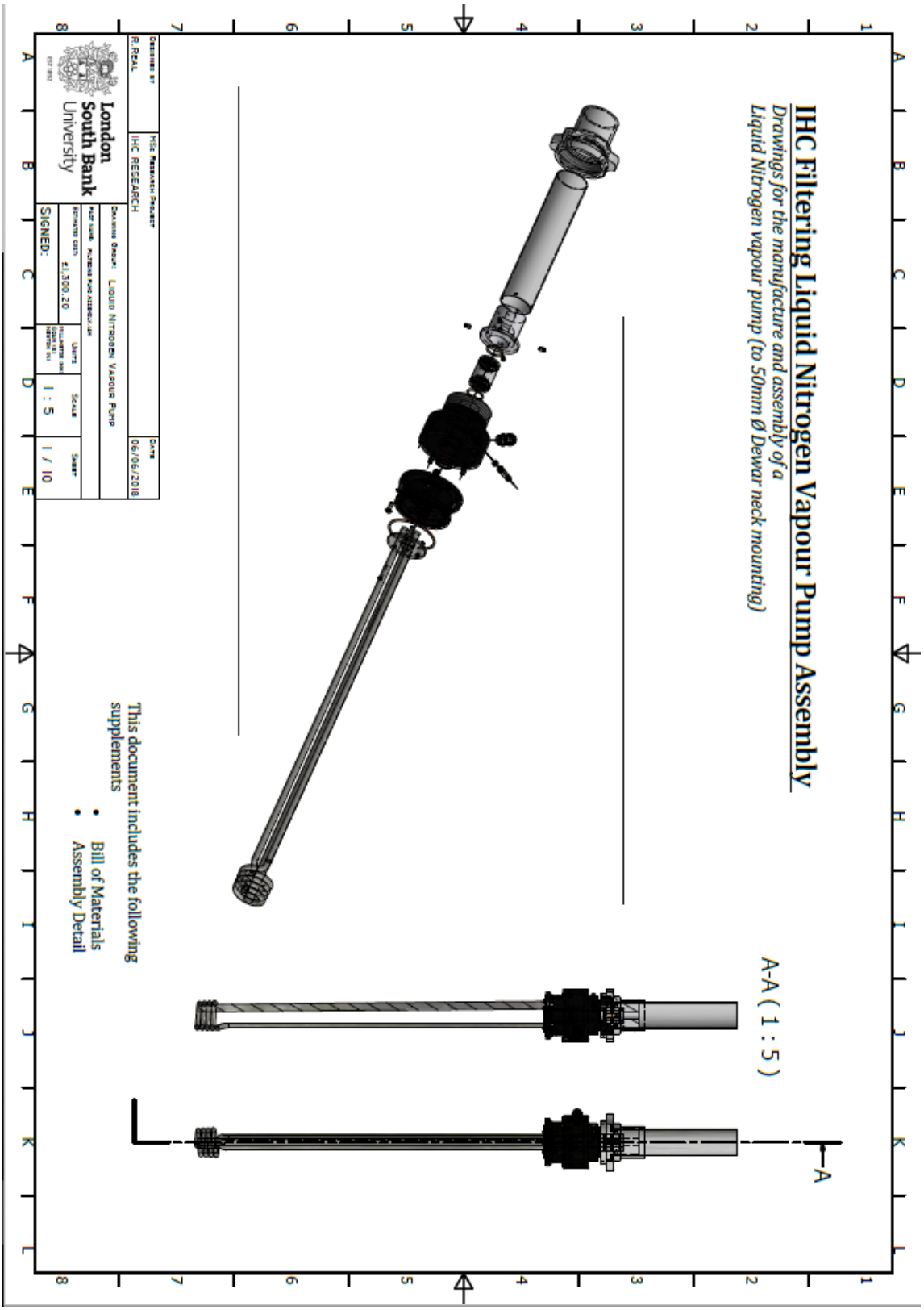
6 Appendix

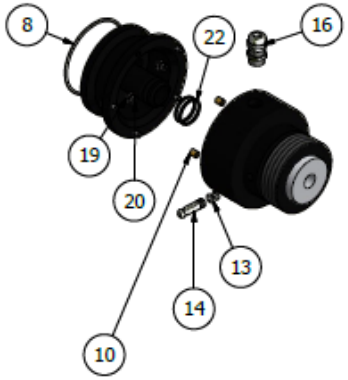
Liquid Nitrogen vapour filtering pump drawings



IHC LN Filtering Vapour Pump General Assembly

Exploded assembly labelled view - General pump assembly - Part list

Internal general assembly pump detail
1:3 Scale - *Reversed view*

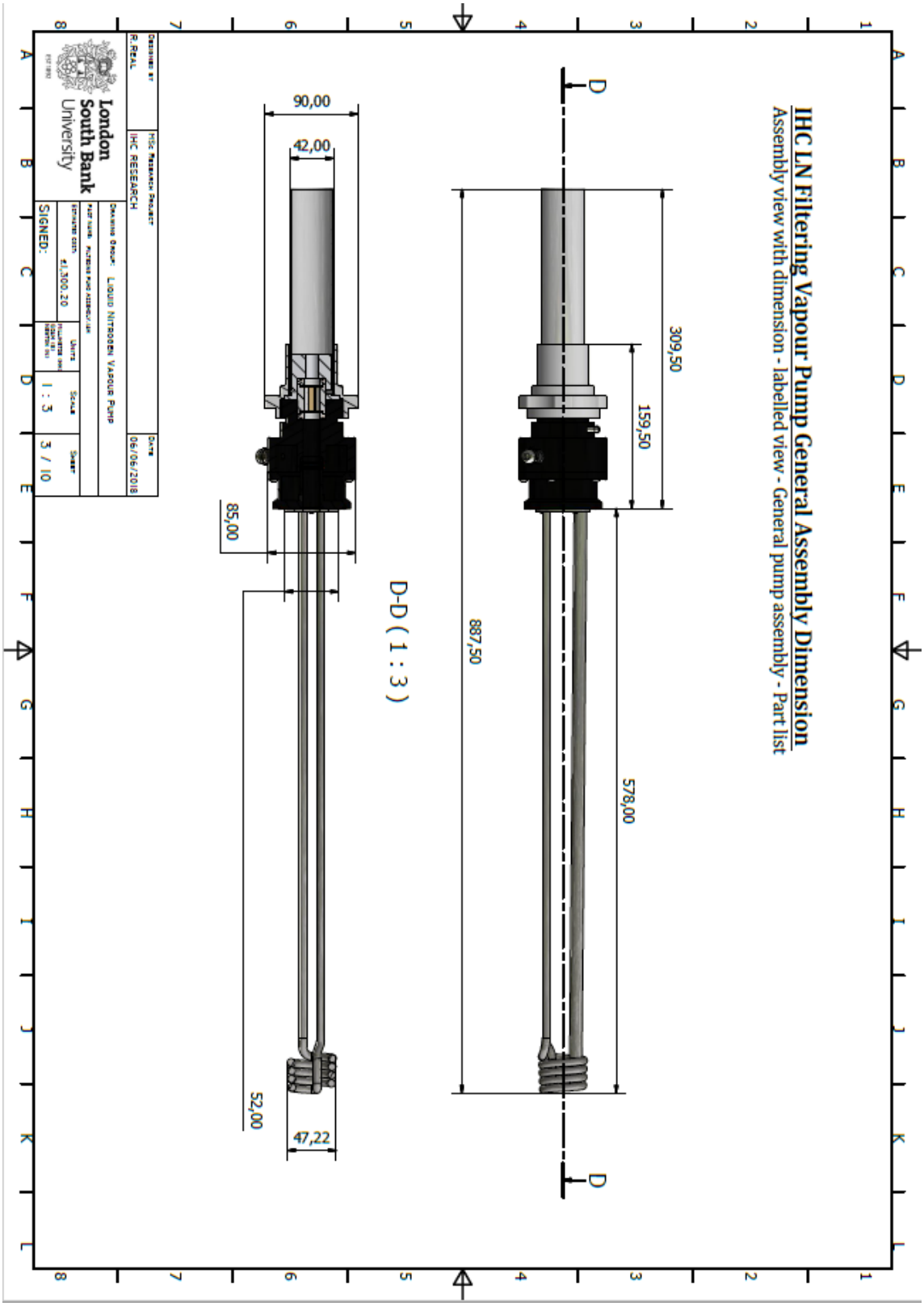


Main body designed to be assembled
With single 3mm (M4) Hex Key

General Assembly

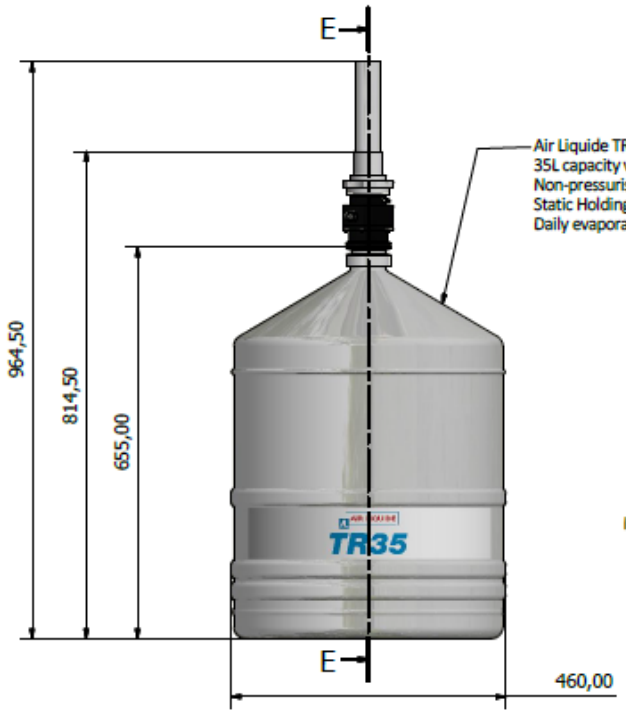
PARTS LIST		
ITEM	QTY	PART NUMBER
1	1	Vapour Filter System
4	2	O-Ring LN Filter
5	1	Heater Coil V2
7	1	Pump Casing lower
8	1	Dewar Mount O-Ring
9	1	Pump Casing Upper
10	5	Threaded Insert M4
11	1	Hose coupling V2
12	1	Hose pump tubing
13	2	Thermocouple mount O-Ring
14	1	Thermocouple Mount
16	1	Power Grommet
17	1	Pump Hose Connector
18	3	Bolt M3 x 0.5 x 20
19	3	M3 Washer
20	3	Nut M3x0.5
21	5	Bolt M4 x 0.7 x 12
22	2	Internal O-Ring
23	4	M4 x 8 Cup Point Grub screw

Designed by	MSc Research Project			Date
R.Real	IHC RESEARCH			06/06/2018
London South Bank University	Drawing Group: Liquid Nitrogen Vapour Pump			
	Part Name: LN Heated Assembly (1)			
	Estimated cost: £1,300.20	Units: Millimeter (mm) Scale (A1) Newton (N)	Scale: 1:6.5	Sheet: 2 / 10
	SIGNED:			


IHC LN Filtering Vapour Pump General Assembly Dimension
Assembly view with dimension - labelled view - General pump assembly - Part list
309,50
159,50
578,00
887,50
D
D
90,00
42,00
85,00
52,00
47,22
D-D (1 : 3)
London South Bank University
R.REAL
IHC RESEARCH
LIQUID NITROGEN VAPOUR PUMP
06/06/2018
1 : 3
3 / 10
SIGNED:

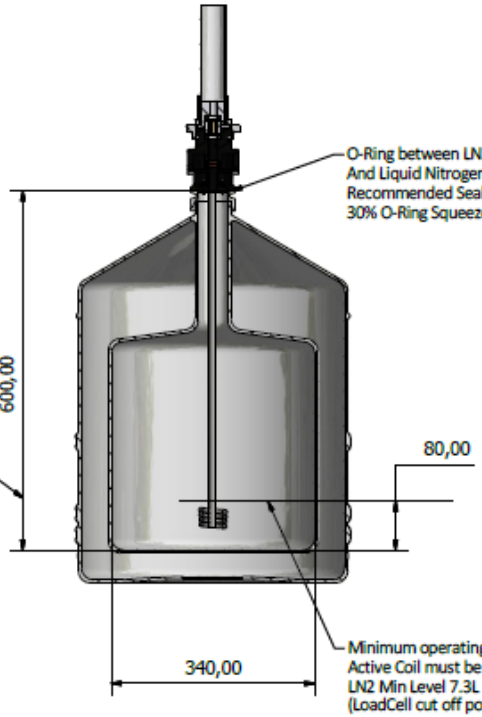
IHC LN Filtering Vapour Pump General Assembly Dewar

Assembly view with Dewar - General pump assembly - Part list



Air Liquide TR35 Dewar Vessel
35L capacity vessel 50mm Neck
Non-pressurised
Static Holding time 125 Days
Daily evaporation rate 0.27L

E-E (1:6.5)



O-Ring between LN2 vapour pump
And Liquid Nitrogen Dewar vessel
Recommended Sealing force
30% O-Ring Squeeze

Minimum operating LN2 Level
Active Coil must be submerged
LN2 Min Level 7.3L
(LoadCell cut off power if LN measure Below)

Designed by	MSc Research Project	Date
R. Real	IHC RESEARCH	06/06/2018

London South Bank University

Drawing Group: Liquid Nitrogen Vapour Pump

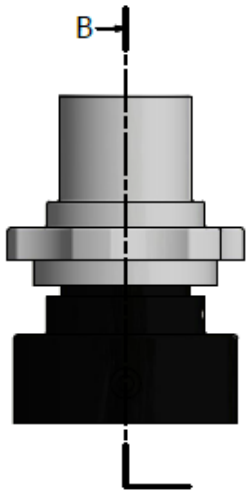
Part name: Heated dewar assembly.iam

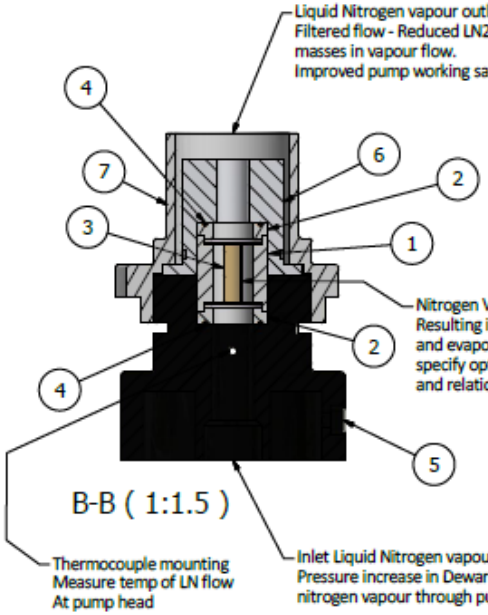
Estimated cost	Units	Scale	Sheet
£1,300.20	Millimeter (mm) Scale (E) Fraction (in)	1:6.5	4 / 10

SIGNED:

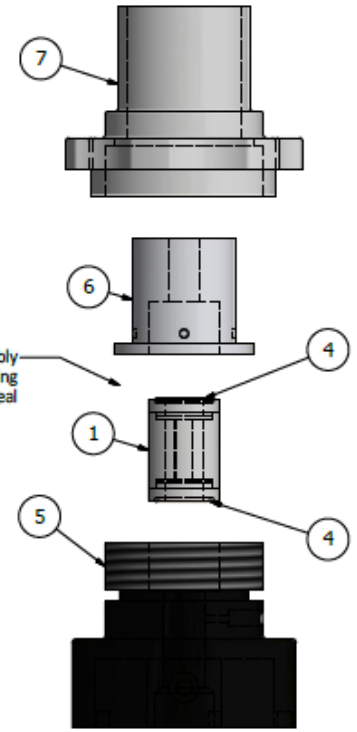
IHC LN2 Vapour filtering system pump assembly

General assembly Liquid Nitrogen vapour filtering system





B-B (1:1.5)



PARTS LIST		
ITEM	QTY	PART NUMBER
1	1	Central Channel Nitrogen Vapour Filter
2	2	End Caps
3	1	Internal Mesh
4	2	O-Ring LN Filter
5	1	Pump Casing Upper
6	1	Hose coupling V2
7	1	Pump Hose Connector

Designed by	MSc Research Project	Date
R.Real	IHC RESEARCH	06/06/2018

London South Bank University

Drawing Group: Liquid Nitrogen Vapour Pump

Part Name: Please Designate Assembly Drawing Type

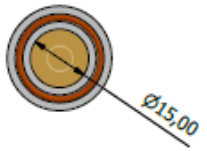
Estimated Costs	Units	Scale	Sheet
£1,300.20	Millimeter (mm) Gram (g) Newton (n)	1:1.5	5 / 10

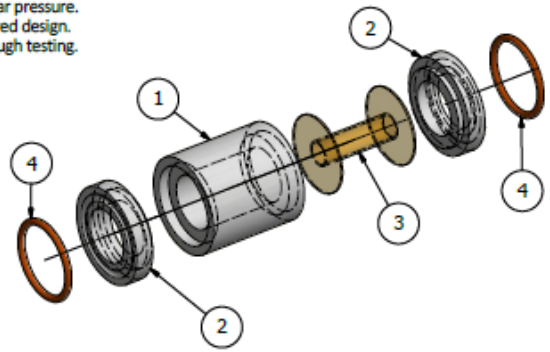
SIGNED:

IHC LN2 Vapour filter assembly

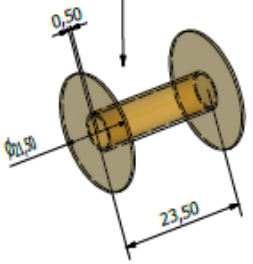
General assembly filtering system

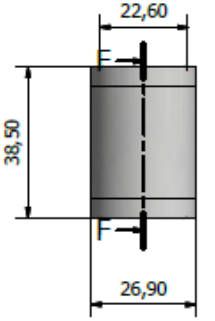
System requires further testing -
Relationship between filter, fluid flow and increased dewar pressure.
Adjustments to be made to heater power output for filtered design.
Specifications for optimum mesh filter to be defined through testing.



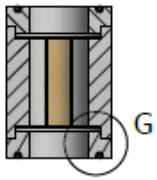


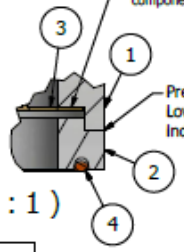
Internal Mesh filter -
Material stainless steel 304/316
Mesh specification to be specified in testing
Mesh Thickness between 0.5mm - 1.25mm





F-F (1:1)



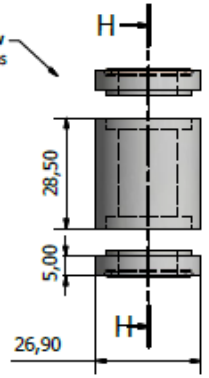


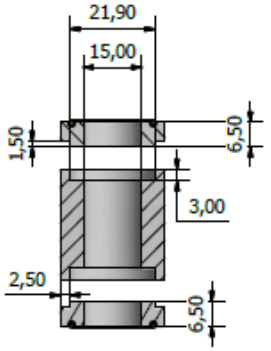
Mesh internal holding structure clamped by joining of external components

Press fit tolerancing
Lower mating surface bonded seal
Industrial cyanoacrylates (Permabond)

G (2 : 1)

Exploded Cartridge View
Filter cartridge Dimensions





H-H (1 : 1)

Designed by: R.Real	MSc Research Project: IHC RESEARCH		Date: 06/06/2018
London South Bank University	Drawing Group: Liquid Nitrogen Vapour Pump		
	Estimated cost: £1,300.20	Units: Millimetre (mm) Scale (1) Section (s)	Scale: 1:1
	SIGNED:		Sheet: 6 / 10

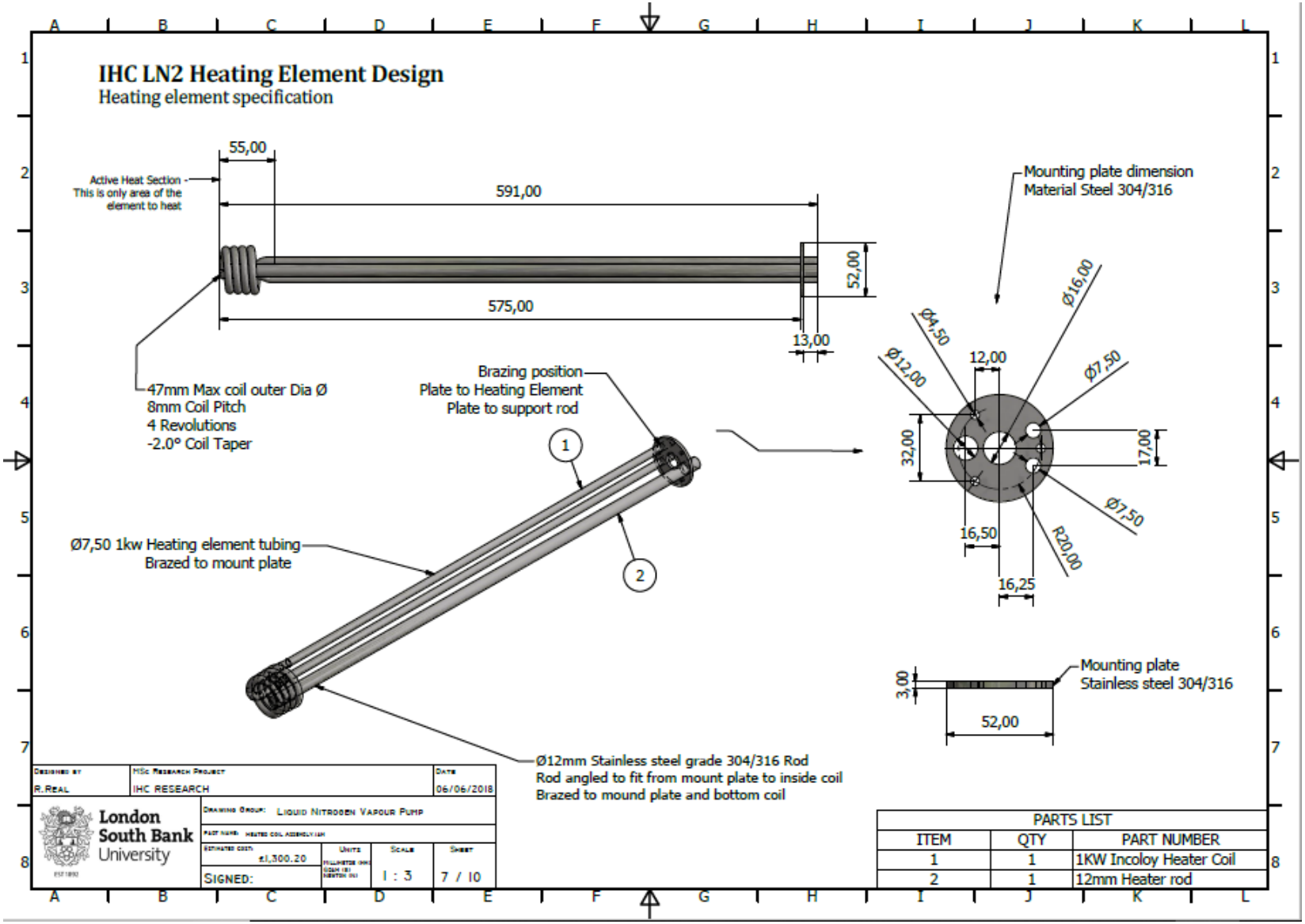
Novel innovation preventing Liquid Nitrogen droplets in vapour flow Improving safety - Protecting user from burns - Potential IP

PARTS LIST

ITEM	QTY	PART NUMBER	DESCRIPTION
1	1	Central Channel	Virgin PTFE
2	2	End Caps	Virgin PTFE
3	1	Internal Mesh	Stainless 304/316
4	2	O-Ring LN Filter	Rubber

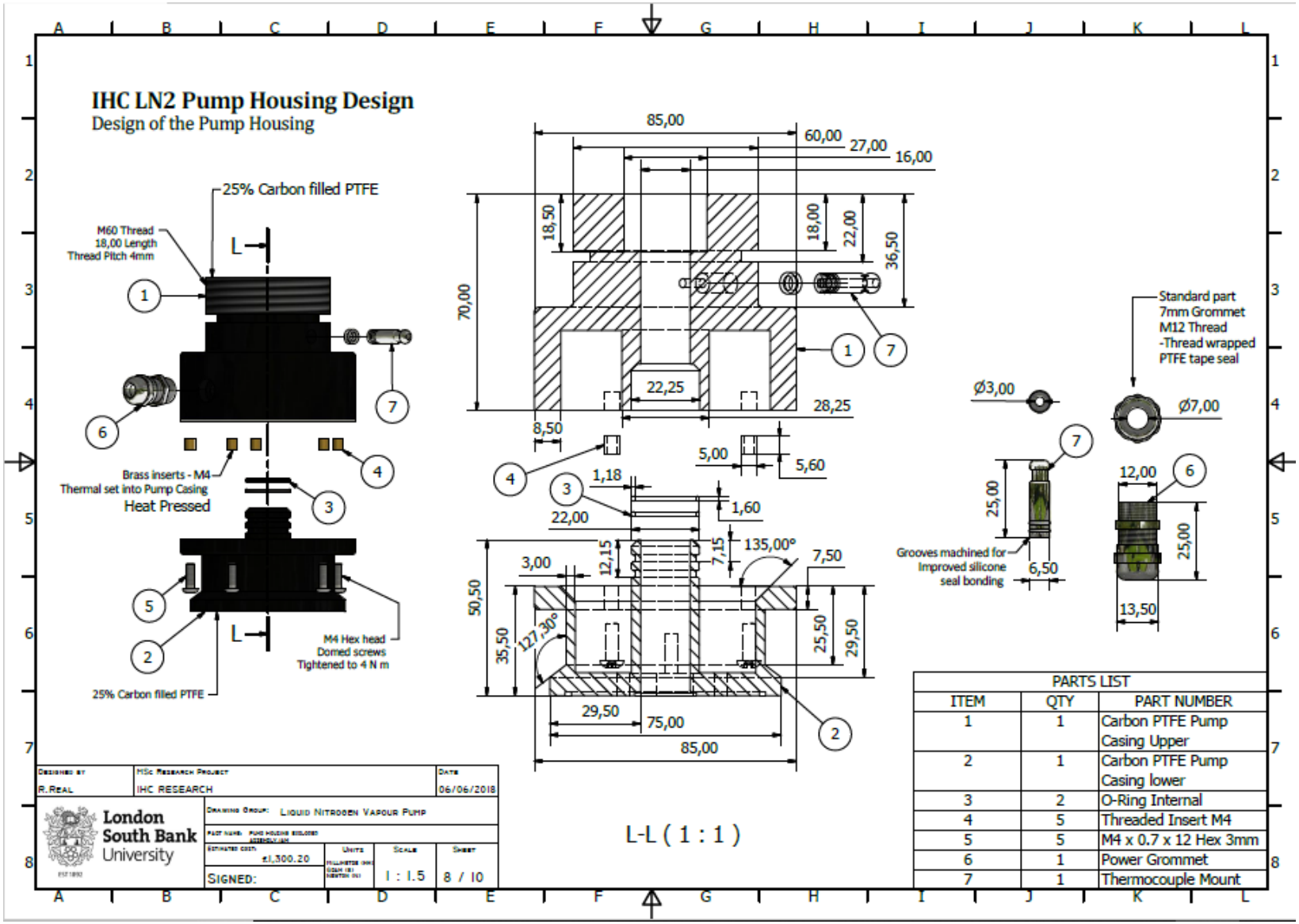
IHC LN2 Heating Element Design

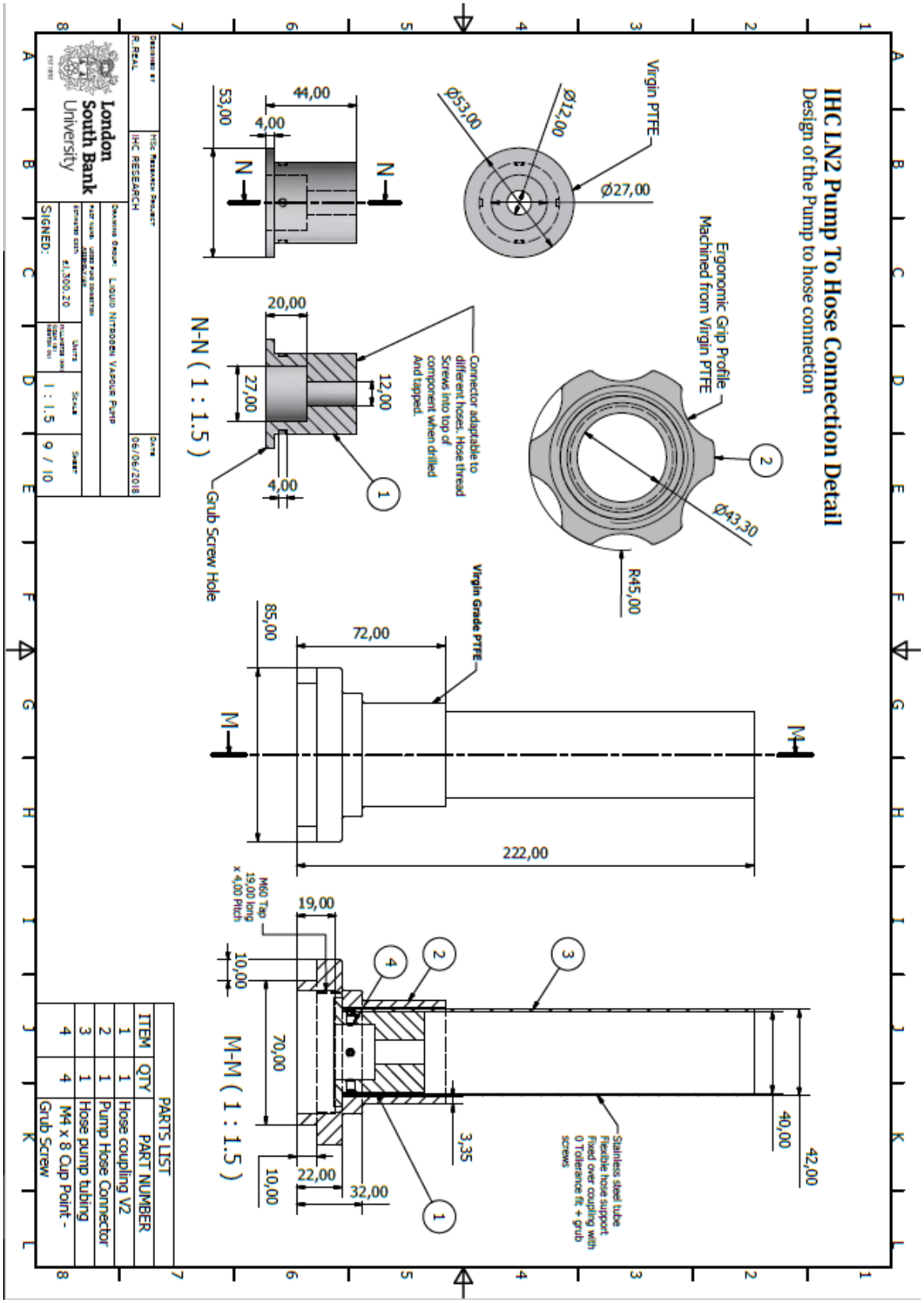
Heating element specification



PARTS LIST		
ITEM	QTY	PART NUMBER
1	1	1KW Incoloy Heater Coil
2	1	12mm Heater rod

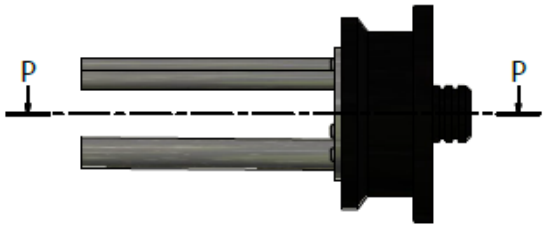
Designed by: R.Real	MSc Research Project: IHC RESEARCH		Date: 06/06/2018
London South Bank University	Drawing Group: Liquid Nitrogen Vapour Pump		
	Part Name: Heater coil assembly.ipt		
	Estimated cost: £1,300.20	Units: millimetres (mm) scale (b) newton (n)	Scale: 1 : 3
	SIGNED:		Sheet: 7 / 10


IHC LN2 Pump Housing Design
Design of the Pump Housing
25% Carbon filled PTFE
M60 Thread
18,00 Length
Thread Pitch 4mm
Brass inserts - M4
Thermal set into Pump Casing
Heat Pressed
M4 Hex head
Domed screws
Tightened to 4 N m
25% Carbon filled PTFE
85,00
60,00
27,00
16,00
70,00
18,50
18,00
22,00
36,50
22,25
28,25
8,50
5,00
5,60
1,18
1,60
22,00
3,00
12,15
7,15
135,00°
7,50
50,50
35,50
127,30°
25,50
29,50
29,50
75,00
85,00
L-L (1 : 1)
Standard part
7mm Grommet
M12 Thread
-Thread wrapped
PTFE tape seal
Ø3,00
Ø7,00
25,00
Grooves machined for
Improved silicone
seal bonding
6,50
12,00
25,00
13,50
PARTS LIST
ITEM | QTY | PART NUMBER
1 | 1 | Carbon PTFE Pump Casing Upper
2 | 1 | Carbon PTFE Pump Casing lower
3 | 2 | O-Ring Internal
4 | 5 | Threaded Insert M4
5 | 5 | M4 x 0.7 x 12 Hex 3mm
6 | 1 | Power Grommet
7 | 1 | Thermocouple Mount
Designed by
R.Real
MSc Research Project
IHC RESEARCH
Date
06/06/2018
London South Bank University
Drawing Group: Liquid Nitrogen Vapour Pump
Estimated cost
£1,300.20
Units
Millimeter (mm)
Scale
1 : 1.5
Sheet
8 / 10
SIGNED:

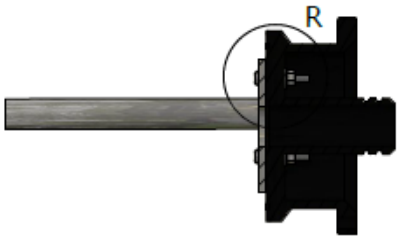

IHC LN2 Pump To Hose Connection Detail
Design of the Pump to hose connection
Virgin PTFE
Ø12,00
Ø27,00
ϕ53,00
Ergonomic Grip Profile
Machined from Virgin PTFE
ϕ43,30
R45,00
44,00
4,00
53,00
N-N (1 : 1.5)
20,00
27,00
12,00
4,00
Grub Screw Hole
Connector adaptable to different hoses. Hose thread Screws into top of component when drilled And tapped.
Virgin Grade PTFE
85,00
72,00
222,00
M-M (1 : 1.5)
M60 Tap 19,00 long x 4,00 Pitch
19,00
10,00
70,00
22,00
32,00
10,00
3,35
40,00
42,00
Stainless steel tube Flexible hose support Fixed over coupling with 0 Tolerance fit. + grub screws
PARTS LIST
ITEM QTY PART NUMBER
1 1 Hose coupling V2
2 1 Pump Hose Connector
3 1 Hose pump tubing
4 4 M4 x 8 Cup Point - Grub Screw
DESIGNED BY R.REAL
HSC RESEARCH PROJECT IHC RESEARCH
DRAWING BRIEF: LIQUID NITROGEN VAPOUR PUMP
DATE 06/06/2018
London South Bank University
PROJECT NAME: HOSE PUMP CONNECTION
ESTIMATED COST: £1,300.20
UNITS
SCALE 1 : 1.5
SHEET 9 / 10
SIGNED:

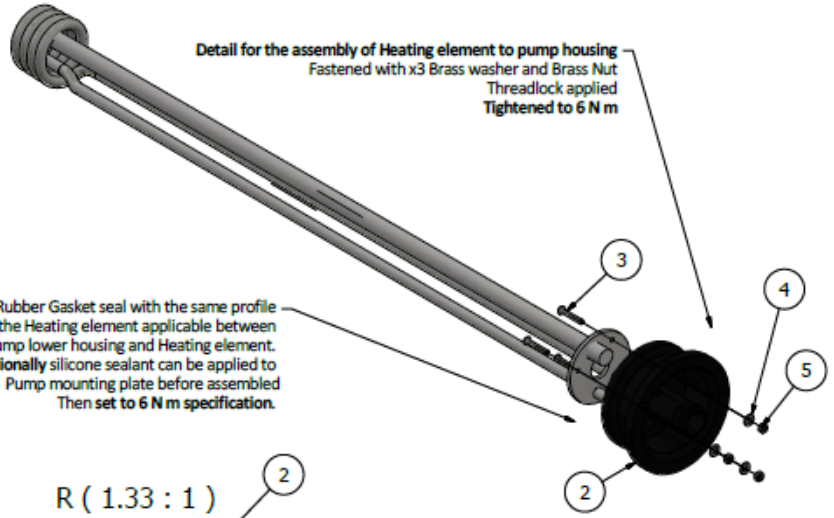
IHC LN2 Housing to heating element fastening

Pump housing to heating element

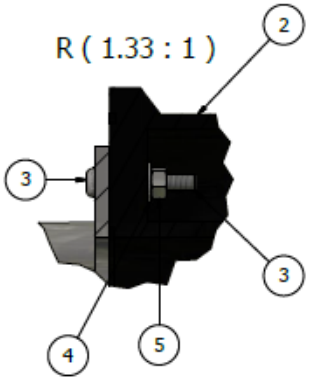


P-P (1 : 1.5)





R (1.33 : 1)



PARTS LIST			
ITEM	QTY	PART NUMBER	DESCRIPTION
1	1	Heater Coil Assembly	
2	1	Pump Casing lower	
3	3	ANSI B18.3.4M - M3 x 0.5 x 20	Broached Hexagon Socket Button Head Cap Screw - Metric
4	3	AS 1237 - 4	Flat metal washers for general engineering purposes (metric series)
5	3	ANSI B18.2.4.2M - M3x0.5	Metric Hex Nuts Styles 2

Designed by	MSc Research Project	Date
R.Real	IHC RESEARCH	06/06/2018

London South Bank University

Drawing Group: Liquid Nitrogen Vapour Pump

Part name: coil to sing mounting ish

Estimated cost	Units	Scale	Sheet
£1,300.20	Millimetre (mm) Gram (g) Newton (N)	1 : 1.5	10 / 10

SIGNED:

Invention Disclosure Form

CONFIDENTIAL

Research, Enterprise & Innovation

INVENTION DISCLOSURE FORM

The purpose of this form is for inventor(s) to provide information about their invention. By completing and submitting this form, you are logging the idea with the University and protecting the intellectual property (IP) rights of staff, students and any others that are involved in the idea. The disclosure is the basis on which discussions will be held with you for the purposes of IP protection and opportunities for commercialisation.

Date of completion of Invention Disclosure Form……18/08/2018……

1	**Title of Invention** ***Liquid Nitrogen Filtering Vapour Pump***
2	**Technical Description** *The Invention as stated above uses a variably controlled heat element to vaporise Nitrogen in its liquid phase (LN2 Liquid Nitrogen) to produce a controlled stream of refrigerated Nitrogen Gas used in clinical procedures to cool skin surface temperature.* *It was observed that pumps currently used in commercial clinical applications draw through the vapour stream droplets of Nitrogen in liquid phase (-196°C) resulting in reported cases of cold burns causing potential damage to tissue through freezing.* *The invention presented in this document improves the safety of Cryogenic Vapour pumps by a means of Vapour stream filtration preventing droplets of Liquid Nitrogen from being drawn through vapour flow onto the target surface.* *The exploded drawings; Attached with this document display an improved system design to increase the device safety.*
3	**Date** *Work on the design of the pump began April 2018*
4	**Awareness of your invention** *Is the invention known about by your line manager, Head of Division or Dean?* *If yes, list those in your School management that are aware of the invention.* *If no, explain why the invention has not yet been discussed.* The invention has been discussed in meetings with both project supervisors and client, Those aware include project supervisor Dr Deborah Andrews, Prof. Graeme Maidment, Dr Katya Mileva, Barney Townsend and Company director Alla Paszynska

CONFIDENTIAL

5	**Inventorship** *Provide details of all inventors involved, including their position and in what capacity they have been involved in the development of the invention.* Ricardo Real – Research student – sole inventor
6	**Employment Status** *Are all the inventors solely employed by LSBU? Yes/No (Please circle)* *If you have answered no please provide details below:*
7	**External Funding** *Was the invention developed in collaboration with an external partner (another university, business etc) or funded by external sources? If yes, please provide details here including details of any contracts that it is subject to.* *The Project is funded by an external partner; Ice Health Cryotherapy ltd. Company number 08408459* *The primary contact being company director Alla Paszynska*
8	**Internal Funding** *Has the invention received funding from any internal sources at LSBU? For example, funding from within your School or Research Enterprise & Innovation?* *If yes, please provide details here: how much was received and what was developed?* No
9	**Past Disclosure(s)** *Have there been any disclosures of the invention? This includes discussions with non-University employees; conference abstracts and presentations; research posters; exhibitions, journal articles; social media and websites in any country.* *No*

10	**Future Disclosure(s)** *Are there any plans to disclose the idea in the near future in any country? If yes, please provide details here.* *No*
11	**Potential Commercial Application and Market** *Provide details of the commercial application of this invention and potential market. You should include details of any companies that are or may be interested in it.* *The pump is to be commercialised by the client; Ice Health Cryotherapy to be manufactured and distributed globally for use in the clinical health and wellbeing market to deliver Cryotherapy procedures.* *Further to this the pump may have potential in the computing industry to cool systems operating at high temperatures without contact.* *Applications may further extend into the applied sciences as a scientific instrument for local cooling requiring contactless application.*
12	**Alternative Use** *Could there be an alternative use for your invention (or a part of your invention) other than the purpose that you originally intended it to be used?* Yes, the invention may have potential use in cooling applications including the cooling of computer/electronics systems and other active low temperature cooling applications.
13	**Prior Art** *Provide information on any patents or literature that you have found that may be relevant to this invention.* An initial patent search for the terms – Liquid Nitrogen Vapour pump, Cryotherapy pump, Cryogenic pump and liquid nitrogen pump returning few relevant results. The most relevant was a patent filed in Poland by Metrum Cryoflex titled – "Method for obtaining a cold gas Jet and the device for obtaining a cold gas Jet" https://worldwide.espacenet.com/publicationDetails/biblio?II=1&ND=3&adjacent=true&locale=en_EP&FT=D&date=20111205&CC=PL&NR=391296A1&KC=A1

	The design of the system is similar in that it uses a heated element to vaporise Liquid Nitrogen however has no features preventing droplets of Liquid Nitrogen exiting the system.
14	**Sources searched** *Provide information about when and where you have looked for prior art or literature eg. Google patents.* *Google Patents* *Espacenet*
15	**Ethics** *Here you should consider whether your invention may require ethical approval (at LSBU and externally) either now or in the future. For example, if human subjects were required to consume or test it.* Ethical Approval may be required in future testing of the invention however at the current stage only performance testing of the pump is to be completed
16	**Other information** *Please provide any other information that may be relevant for IP protection and/or commercialisation*

Inventor Declaration
By completing and submitting this form, you agree that:

- you have fully disclosed the invention;
- the information that you have provided is accurate to the best of your knowledge;
- all inventors have been declared;
- you will co-operate with SBUEL to seek IP protection and opportunities for commercialisation

Inventor 1

Print Name……Ricardo Real ……..Signature……

Phase 2 – Market Research Report

'A review and analysis of the Cryo-Tech health market, determining areas of value and identifying opportunities for new product development'

Company: Ice Health Cryotherapy
Product: Combined Cryo EMS unit
Market research period: To September 2017

Prepared by R. Real
London South Bank University

****** Special Notice******

The information in this Market Report is sourced from publicly available records and accurate at the time of publication.

Background Information

With a growing body of research into the applications of cryogenic technology and the adoption of its uses as a healthcare resource a leading cryotherapy clinic and distributor have commissioned a study exploring the potential benefits of stacking technologies and the opportunities presented to innovate within the healthcare market by doing so.

Currently there are two widely available Cryo-tech health treatments on the market; Cryotherapy a procedure for sports injury and recovery, and Cryolipolysis a procedure developed to non-invasively reduce localised areas of body fat as an alternative to Liposuction, an invasive localised treatment. Both Cryotherapy and Cryolipolysis have seen significant growth in exposure in recent years, endorsements by Celebrities, Athletes and sporting organisations have led to a surge in demand for Cryo procedures and a rapidly growing consumer driven market.

Given the global exposure the industry has been subject to, manufacturers are faced with a competitive market. Although the primary consumers of Cryotherapy units have traditionally been health clinics, beauty salons and medical practices; a new consumer driven trend is defining an emerging market within the healthcare industry of personal home use cryogenic machines.

The Client Ice Health Cryotherapy a health and wellbeing Cryotherapy clinic and Cryogenic equipment distributor has been a long-term provider of both localised and whole-body Cryotherapy procedures and discovered that the combination of Electro Muscle Stimulation with Cryotherapy could present potential to innovate within the Cryo-tech health market being the first to introduce a commercial combined Cryo-EMS unit.

The company having successfully conducted preliminary research into the physiological benefits of a combined Cryo-EMS procedure at London South Bank University and are now looking to develop a prototype unit exploring the combination of Cryo technology with EMS and heat and its market potential.

This report aims to identify the opportunities within the Cryo-tech health market presenting most potential for impactful innovation in new product development.

Research Methodology

The market research was conducted throughout the third quarter of 2017 by R. Real, London South Bank University. The information is of a proprietary nature to the research sponsor Ice Health Cryotherapy and not to be publicly distributed without the appropriate express permission of the research sponsor.

The report contains information from a range of sources including:

- *Information accessible through Annual Reports and Government Reports available for public review.*
- *Company Marketing, Advertising and Press releases including publicly available information from both national and international independent media publications.*
- *Subscription based market reporting i.e. Mintel*
- *Openly available online research including third party referencing*
- *Trade related union publications and directories including online forums*
- *Open access online consumer market forums and business forums*

Sources of information were assessed prior to being considered for this document and efforts made to insure information is accurate and within relevance, however given market volatility and development the conclusions drawn from this report may be subject to review in the future.

Table of Contents

I – A Brief History of the Cryogenic Health Industry

The term Cryotherapy was derived from the Greek, Cryo meaning cold and therapy meaning cure with its uses as a medical treatment documented as early as the 17th Century.

Most prominently Cryotherapy is employed as a surgical treatment acknowledged by medical professionals as Cryosurgery. Used in the destruction of abnormal or diseased tissue and the dermatological treatment of skin conditions such as Warts, Solar Keratosis and Moles as a low risk, rapid and efficient outpatient procedure. (*The Cryosurgery procedure involves the localized application of Liquid Nitrogen through an applicator nozzle rapidly freezing tissue on a cellular level*)

Historically, the properties of cold water submersion and Ice compression have been applied for their benefits to health including: Improved recovery, slow cell aging, decreased pain and muscle spasms and general wellbeing thus leading to the development of technological Cryotherapy products including localised Cryotherapy units and whole body Cryo saunas/chambers exposing patients to regulated Liquid Nitrogen or refrigerated cold air at a constant temperature stream of up to -186°C for a period of time relative to the treatment type and area, creating ideal conditions to achieve the desired physiological responses and results.

A more recent Cryogenic development introduced to the Cryo health market is Cryolipolysis a non-invasive body sculpting procedure growing in popularity as an alternative to invasive contouring procedures such as Liposuction. The theory behind Cryolipolysis emerged after a correlation was found between cases of panniculitis in the cheek and the eating of popsicles. A procedure based on this principal was developed in 2008 by Zeltiq Aesthetics and successfully tested in a porcine model before proceeding to human trials, replicating the previous successes in reducing local subcutaneous adipose tissue (Fat).

Zeltiq subsequently developed and launched the Cryolipolysis procedure and CoolSculpting technology. Zeltiq remains the market leader in Cryolipolysis and was recently acquired by BOTOX manufacturer Allergen PLC to supplement their range of clinical aesthetic products for a reported $2.48 Billion.

The use of Cryo technology has also found a niche in the post-surgical medical market as a means of pain relief, with studies documenting the efficacy of combing Electro Muscle Stimulation with Cryotherapy to enhance the anaesthetic effects of localised cooling post-surgery, although, few studies have been conducted into this area and remains subject to future research and development.

II – Analysis and Review of the current Cryo Health Market

Cryogenic Health Market; Overview

The Cryogenic Health market includes industries and consumers concerned with providing treatments under the Cryotherapy and Cryolipolysis categories.

A September 2017 Mintel report on the Spa, Salon and in store treatment sector, the largest consumer of Cryogenic health technology indicates that the market is subject to a 1% growth by the end of 2017's fourth quarter, taking the overall UK market value to £7.57 Billion and growing by a further 8.1% to £8.19 Billion by 2022 with analysts claiming growth to be driven by the development of technological treatments encouraging consumer experimental spending.

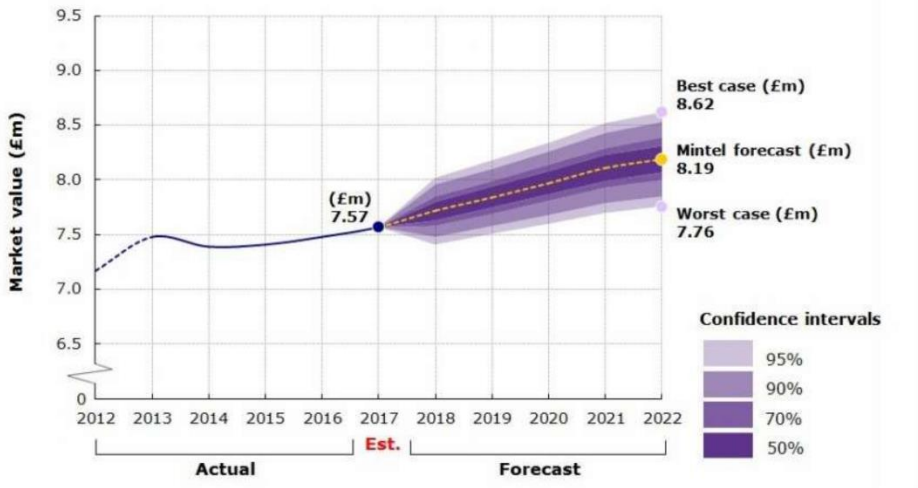


Figure 1 - Mintel Report Spa, Salon and in store treatment market projection September 2017

A further report published by Persistence Market Research in January 2017 focused on the global Cryo-Health market supports the Mintel market projection, further projecting continued market growth to 2024.

PricewaterhouseCoopers, PwC, a multinational data analysis and advisory firm have observed health sector movements and published in February of 2016 a report titled; "Capture the Growth; The opportunities for new entrants in healthcare and wellbeing"

The report identifies significant market potential with the Rt Hon Alan Milburn from the health industries oversight board stating;

"The time is ripe for new ideas in UK healthcare. Some of those new ideas and solutions will come from new sources – organisations which traditionally have not been involved in healthcare, fitness or wellness. Worldwide, the players on the healthcare pitch are changing. And the UK is no exception. New entrants are emerging, disrupting the old ways of doing things."

The report further outlines the challenges facing new market entrants and opportunities enabling healthtech market growth in the infographic below.

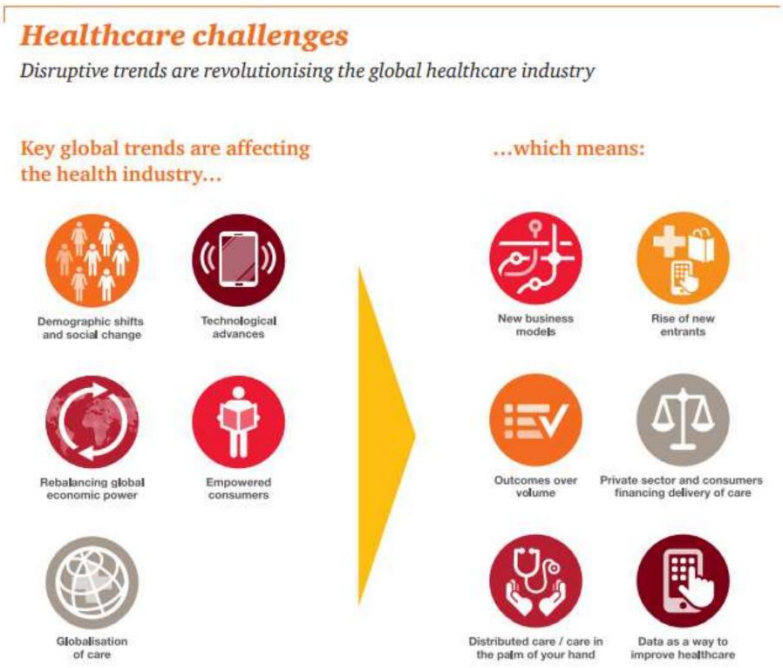


Figure 2 – Healthcare challenges, Capture the Growth; The opportunities for new entrants in healthcare and wellbeing, PwC February 2016

The statements put forth by PwC are supported by the current technological revolution in healthcare; driven by Mobile technology, Artificial intelligence and the internet of things (IoT) creating new opportunities for novel innovations in the Health Technology market.

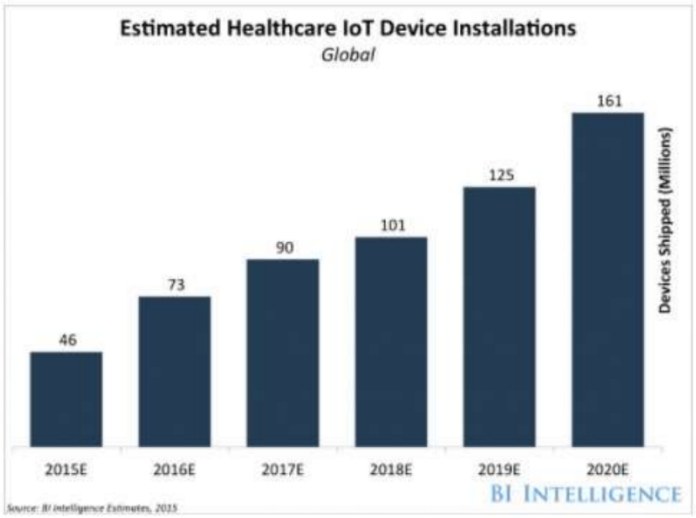


Figure 3 Business Insider estimated healthcare IoT device installations

Figure 3 above, a graph published alongside an article from Business Insider on the IoT healthcare technology market displays an estimate of global IoT healthcare device installations, projecting 161 million devices shipped in 2020 and a market valuation expected to top $400 Billion USD by 2022.

This indication of a mass market adoption of health technology is enabling procedures such as Cryotherapy and Cryolipolysis to integrate with the broader healthcare technology market.

A separate publication by Tällt ventures reviewing healthcare market disruption suggests healthcare to be the fastest growing technology market, identifying five areas key to growth;

- Personalised Health
- Wearables
- Telemedicine
- Professional Healthcare
- Healthcare efficiency

Health and Beauty consumer behaviour and attitudes –

A study conducted in January 2017 exploring consumer behaviour and motivators behind health and beauty consumer spending through an online questionnaire of 651 participants identified the leading motivator to undergo a treatment across genders was self-reward followed by special occasions.

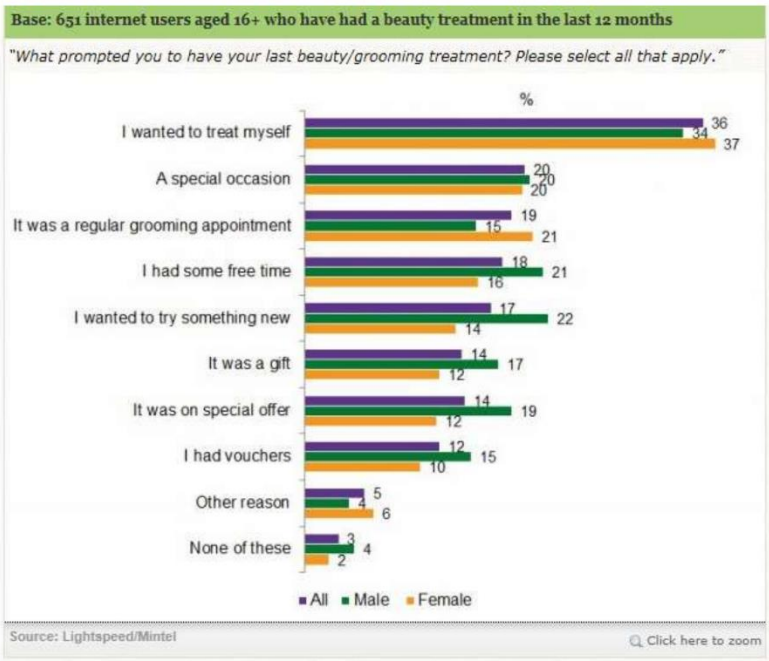


Figure 4 - Reasons for having last beauty/grooming treatment, by gender, June 2017. Mintel report September 2017

Although the study outlined in figure 2 doesn't factor benefits to health as a motivator behind consumer consumption it's evident that the principal Cryotherapy procedure market is heavily dependent on 'experience' spending and thus the availability of disposable income; therefore, susceptible to volatility and periods of slower market growth relative to the economic climate.

Cryogenic health treatments are however relatively unfamiliar amongst the mass populous, but, due to the use of technology by public figures and the correlated growth in consumer interests, the Cryotherapy market has seen increased mainstream attention, potentially compensating for periods of slower economic growth through an increasing procedure awareness and marketing; validating analyst Cryo-health market projections.

A further topic of interest discussed on consumer behaviour in the September 2017 Mintel report identifies a strong emerging trend of consumers expecting services to be brought to them; a mobile economy in which therapists make home calls for on-demand services.

The Health and Beauty industry is seeing a rise in mobile treatment apps offering therapists additional income to full time salon work with analysts predicting an increase of experienced therapists leaving the salon and clinic industry to set up independently or provide mobile services.

However a June 2017 market research survey of 2000 online participants sees consumers emit therapists altogether as the results published in figure 3 show a positive consumer attitudes towards DIY treatments favouring value offered by 'do it yourself' alternatives.

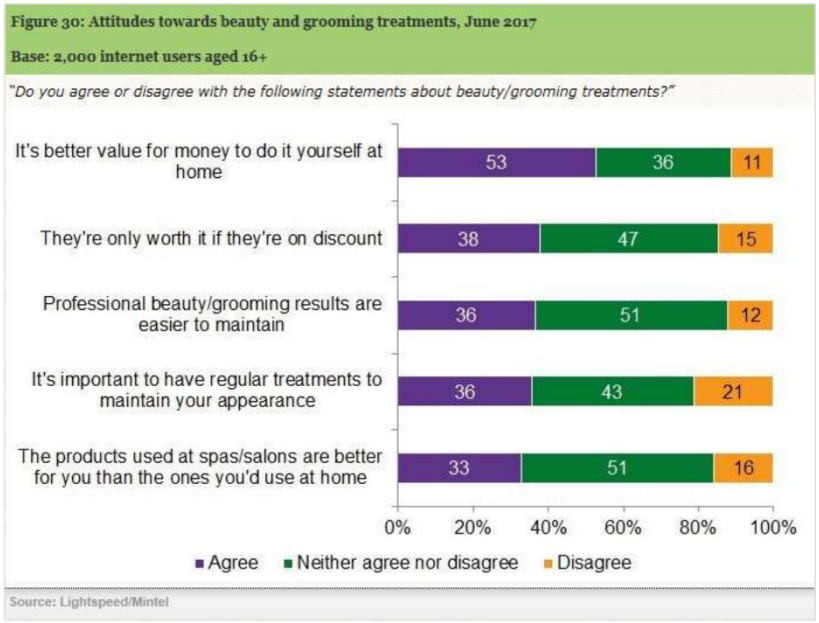


Figure 5 Attitudes towards beauty and grooming treatments, June 2017

The consumer trends displayed above are gradually being reflected in the Cryogenic health product market with portable and home use cryotherapy and Cryolipolysis machines being introduced throughout online marketplaces such as Alibaba, Amazon and eBay; listed under names such as 'Fat freeze machine, slimming belt and cryotech' priced significantly under professional Cryolipolysis units, suggesting a potential emerging technology trend.

The data below from a Phillips survey represents consumer attitudes toward healthcare technology highlighting statistics to framing consumer health tech attitudes.

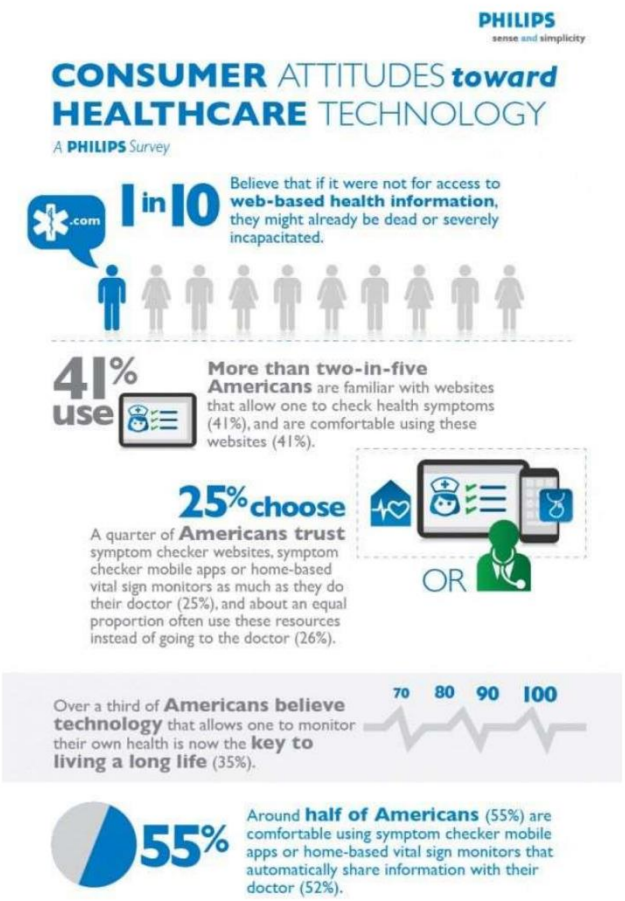


Figure 6 Phillips survey – consumer attitudes towards healthcare technology

The survey indicates stable consumer adoption of healthcare technology; identifying over a third of Americans to consider healthcare technology as now being key to prolonging their personal health and wellbeing.

Attitudes therefore embracing healthcare technology are translating into consumer health consciousness, further presenting evidence for a strong future health tech market.

An area previously defined by Tällt ventures as key to the emerging HealthTech industry is personalised health, enabled by sensors and AI (artificial intelligence) to deliver optimised personal treatments. A supporting article from Forbes magazine titled "How Machine Learning, Big Data and AI Are Changing Healthcare Forever" states;

"While robots and computers will probably never completely replace doctors and nurses, machine learning/deep learning and AI are transforming the healthcare industry"- Forbes

Research into consumer attitudes towards AI and Machine Learning in healthcare is publicly limited, however the subject may become a significant influencer behind health technology consumer attitudes.

This observation was further supported by former Facebook employee Elizabeth Linder during a conference on the Internet of Things at the Royal Society outlining consumer demand for technology driven by AI; providing better, faster optimised results. The example was given of a futuristic wearable fitness exercise monitor, expected to measure current heart rate, calculate a target heart rate from biometric information and have a built in personal trainer monitoring performance and providing instruction, on demand as and when required.

Smart Personal technology remains a topic of significant market interest as consumer attitudes begin assigning value to AI products offering better, faster, personal results.

Cryogenic Health market overview summary

From the research, it's evident that the analyst consensus projects stable Cryogenic and health market growth with the revolution of health monitoring and personalised health technology complimenting and potentially accelerating market growth rate and user adoption.

Emerging consumer and technology trends are presenting opportunities for new entrants to innovate through technological development bringing to market the next generation of healthcare technology.

The following tables outline opportunities and risks presented to new product development in the cryogenic health market with a ranking out 5 identifying strength.

Markets Opportunities	Strength
Demographic shifts and social change – Consumers embracing healthcare technology.	5
Technology Advancements – Artificial intelligence, Machine learning, Big Data and the internet of things creating new market opportunities.	5
Personalised Healthcare – Consumer attitudes shifting from general to personalised procedures.	5
Mobile Treatments – Consumers adopting mobile treatments enabled by mobile applications.	5
New Business Models – Redefined business models, creating a demand for product innovation allowing market growth and new business development.	4
Market Risks	**Strength**
Rapidly Changing Markets – Rapidly changing consumer markets and attitudes leading to shorter market trends and faster product turnover.	2
Empowered Consumers – Consumers shifting towards do-it-yourself alternatives through availability of online documentation.	2
Influx of Competitors – The markets strength could lead to more competition in the Cryogenic health sector.	2
Economic Conditions – Periods of slower market growth relative to the economic climate.	2

Table 1 Market Risks vs Market opportunities

The following section of the report analyses Cryogenic health industries; further identifying risks and opportunities presented in each to innovate through new product development.

- **The Cryolipolysis industry**: Non-invasive cosmetic weight loss, body shaping
- **The Cryotherapy industry**: Injury therapy, improved recovery and wellbeing

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The Cryolipolysis Market Overview–

Cryolipolysis has established itself as a non-invasive alternative to the popular body sculpting procedure; liposuction, offering the localised reduction of subcutaneous fat, body contouring and definition of areas such as the Abdomen and Flanks without the need of anaesthetic or minor surgery.

The standard Cryolipolysis procedure consists of a predetermined area of tissue being drawn into a vacuum applicator and cooled using sensor driven thermoelectric plates to temperatures of between +5/ -5°C for a period of approximately 1 hour; resulting in a permanent local body fat reduction of up to 25% within two to three months of the initial procedure.

Figure 7 - Zeltiq CoolSculpting Cryolipolysis unit

The Cryolipolysis procedure is limited to a market of consumers within approximately 13.5kg of their target body weight as research has shown the procedure to not be as effective in cases of excessive fat (adipose tissue) therefore limiting its use as a medical resource and restricting the procedure to the cosmetic market; although with further Cryolipolysis research and development the procedure may present value as a resource to the medical obesity treatment market.

Combined Cryolipolysis and Electro Muscle stimulation units are in production however as packaged as a bundle of technologies including Cavitation, Radio frequency, Laser, Bio electric stimulation ect and do not exclusively explore the combination of Cryolipolysis with Electro muscle stimulation and its potential benefits.

Cryolipolysis market

Recent Cryolipolysis technology investor Allergen stated body contouring to be a market opportunity worth $4 Billion dollars per annum after acquiring leading Cryolipolysis device manufacturer Zeltiq Aesthetics in 2017 for $2.48 Billion Dollars.

Further to this a report previously referenced in the market overview titled 'Capture the Growth' by PricewaterhouseCoopers identifies consumer weight loss to be amongst the strongest growing healthcare markets with a projected increase in consumer spending of 17% by 2020 and a UK market valuation of £2.1 Billion GBP.

Figure 8 Healthcare spending, Capture the Growth; The opportunities for new entrants in healthcare and wellbeing, PwC February 2016

A global Industry analysis and forecast for 2017 to 2025 of the slimming device market by Persistence market research states that "Increasing slimming device adoption will surge the market growth by 2025".

This statement is further supported by market researchers Data Bridge identifying the drivers behind the global slimming device market to be an "increasing obese population" and "rising awareness regarding health and fitness".

Figure 9 Data Bridge Market Research - Global slimming devices

The report additionally discloses a market revenue growth projection (CAGR) for slimming devices of 9.5% between 2017 and 2024 from a global $7.4 Billion USD revenue in 2016.

The projection for slimming device market growth correlates with the identified increase in weight loss consumer spending (figure 8) indicating slimming devices to account for a significant proportion of the overall weight loss market and continue contributing to market growth as consumer attitudes shift to embrace healthcare technology.

The unanimity of market reports suggest a strong upward market trend, indicating continued future market growth over the next 5+ years.

Cryolipolysis pricing review -

Cryolipolysis procedures range between £75 to £750+ per treatment area with prices increasing relative to the amount of areas simultaneously treated and the reputations of both clinic and Technology on offer.

The rising demand for multiple simultaneous procedures has driven the development of higher performance machines with multiple applicator outlets, delivering simultaneous procedures without the additional investment of capital and space to a secondary Cryolipolysis unit.

Figure 10 – Four Handle Cryolipolysis machine

From analysing procedure retail prices, a positive correlation is apparent between procedure cost and brand strength; with clinics assigning a higher retail price to products backed by research and intellectual property.

The initial investment into a market leading Cryolipolysis unit can be significantly higher than alternative products however the marketability and brand power presented by market leaders promise a self-sufficient investment, attracting consumers from the brands treatment network based on brand exposure and reputation.

In recent years the Cryolipolysis market has seen an influx of lower cost clone machines offering similar benchmark specifications to market leaders for lower upfront costs through online marketplaces such as Alibaba.com allowing small to medium health and beauty enterprises to integrate Cryolipolysis as a procedure to their revenue stream.

The barrier to market of initial investment for SME's is therefore alleviated and due to this providers can be flexible with procedure retail pricing to match consumer demand and market trading conditions.

To conclude from the above points, it's clear that procedure pricing and thus product value is relative to brand power; built on research activity, accreditation and validity, attributing a higher retailing procedure price to products with more background research activity.

Market Leaders	Unit cost (approx. £GBP)
Zeltiq Aesthetics – CoolSculpting	£70,000 +
3DLipo – 3D Ultimate	£32,000 +
Lovelite – Lipogaze	£12,000 +
CLATUU – CLATUU 360	£30,000 +
Value products	**Unit cost (approx. £GBP)**
NEWANGEL – CRYO6S	£1200 +
HONKON – IPO-E	£2600 +
PZ LAZER – PZ838/CoolSlimming	£2600 +
NUBWAY – ICE SHAPING IV PRO	£4500 +

Table 2 - Price Comparison Market leaders vs Value

The table above compares Cryolipolysis market leader unit prices with value replications. This analysis supports prior claims that unit value is relative to brand strength.

Consumer Profiles: The target consumer –

The following consumer profiling aims to identify the ideal Cryolipolysis procedure target consumer.

The strategies employed behind Cryolipolysis treatment marketing share a common consumer profile, a demographic of working professionals in search of procedures effectively addressing areas of dissatisfaction without the investment of time.

Although a large percentage of Cryolipolysis consumers are female, a growing number of consumers undergoing Cryolipolysis are male with popular treatment areas including the Abdomen, flanks and arms. Therefore, the significance of gender neutrality in product development and marketing should be highlighted.

Profile Category	Profile Group	Target Procedure Consumer
Cryolipolysis Demographics	Age	25 to 55
	Gender	Neutral predominantly female
	Income	Mid to High income £25k+
	Culture	Western.
	Family Cycle	Single or married with family
	Work	Client based jobs, sales, people, media, public eye, city, office, travel, no job.
	Education	Higher education, secondary school, College, University.

Profile Category	Profile Group	Target Procedure Consumer
Cryolipolysis Psychographics	Lifestyle	Social, events, functions, working professional, digitally active, media consumer, social media, following new trends and news.
	Concerns	Concerned with, appearance and wellbeing, self-esteem, managing time, Positivity, aging, image.
	Opinions, Attitudes, Interests and Hobbies	Goal driven, open to experience, active on social media, new trends, celebrities, health and beauty, blogs, reality television, curious.
	Degree of Loyalty	Brand loyal, quality/image over value, Lifestyle brands, willing to try new trending products.
	Occasions to undergo a procedure	Weddings, holidays, experience purchases, self- reward, to relax, boost self-confidence/esteem.

Table 3 Consumer profile Cryolipolysis

The tables above categorise the procedure consumer into a selection of demographic and psychographic metrics allowing to further analyse factors influencing shifts in consumer attitudes and therefore opportunities for innovation in new product development.

Consumer Demographics Points of interest -

Looking further into consumer demographics a point of interest and debate is age with it being argued that the younger demographic of 18-30 year olds across genders are increasingly adopting the popular gym, health and fitness trend, enabled by the rise of budget gyms offering affordable unrestricted access to 24/7 facilities, this, coupled with the influence of social media on the ideals of image and lifestyle is resulting in the emergence of a an exercise culture amongst this demographic.

The identification of a fitness trend amongst the younger demographic could be an indication that the Cryolipolysis market may be at risk of future health-conscious consumers no longer requiring slimming procedures.

A report however by the World Health Organisation (WHO) shows whilst use of health and fitness establishments have been increasing, so have both childhood and adult Obesity rates with 39% of adults 18 or over worldwide reported overweight in 2014 by the WHO.

A stronger primary target consumer was therefore identified; the 30 to 55-year-old demographic of working professionals; a time conscious consumer spending on self-esteem, wellbeing and the packaged clinic experience; experimenting with the latest marketed procedures to offer rapid results.

A further point to highlight from the consumer demographic is the identification of a 'Western image' ideals, to further explore this concept the consumer environment must be considered, encompassing other demographic profiling points such as work and education to build the model of a 'modern society' upon which the Cryolipolysis market has been established.

'The target consumer identified are competitive individuals, educated to the relevant professional level and driven by success in terms of career, personal ambition, societal status and image. Given the societies in which the consumer exist, ideals of image are defined by the media, advertising and social platforms with high frequency engagement, enabled by personal mobile technology, leading to shorter intense market trends and volatile markets with a high product turnover rate, bubbles.

The consumer is conscious of emerging trends and therefore willing to experiment with procedures to maintain a culturally defined image, identifying with trends coinciding best with personal ideology and social standing, thus a one-off procedure promising rapid results to achieve a desired image presents strong market potential.'

Figure 11, a statistic published in a Jan 2017 report by We Are Social and Hootsuite geographically locates the demographic by assessing global social media penetration to identify the largest markets of digitally engaged consumers.

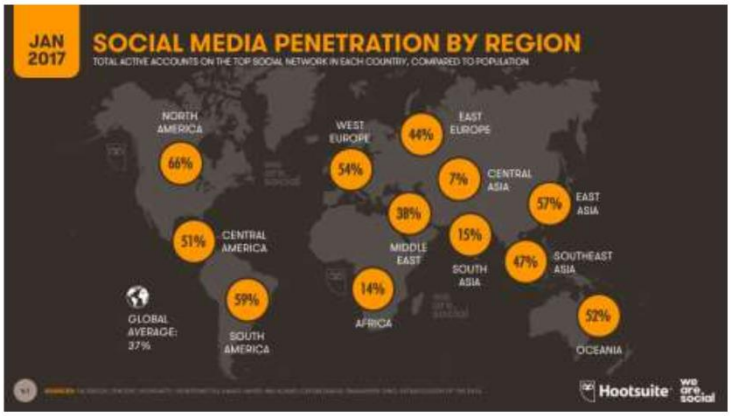

Figure 11 – Wearesocial – Social media penetration by country 2017

The infographic shows North and South America, Europe and Asia to have the highest concentration of digitally engaged consumers reachable through digital and social media marketing.

A further geographical assessment allows a correlation to be defined between social media penetration and disposable income, a statistical infographic, figure 8 below published by Numbeo, a crowdsourced data group presents a metric of geographical disposable income.

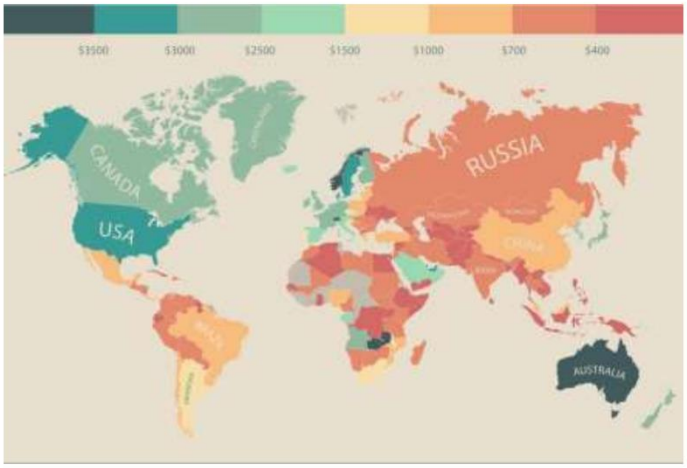

Figure 12 – Monthly Disposable income heat map Numbeo

Analysing both statistics from figures 7 and 8 a positive correlation emerges between demographics with higher monthly disposable incomes also displaying a higher media engagement rate, identifying large potential consumer target market pools and a route to reaching the consumer through digital marketing campaigns.

The Cryolipolysis Technology consumer: Clinics, Spa's and treatment providers

The technology consumer market consists of clinics, Beauty salons, spa's and a growing number of mobile or independent therapists.

In the interests of technology consumers are: emerging trends, product marketability and added value, enabling business growth and higher revenues.

The table below outlines the needs of technology consumers (Tertiary sector) from new product development.

Consumer	Product needs
Tertiary sector – (health clinics, beauty clinics, spa's, therapists, mobile therapists, salons)	Offer significant innovation or marketability to compete with existing technology.
	Present value as an investment capable of increasing revenues through procedure sales; contributing to business growth.
	Backed by research and development increasing consumer confidence and procedure marketability therefore adoption.
	Developed alongside emerging social trends, encompassing the market direction and consumer attitudes to deliver disruptive products and present potential for future market growth and segmentation.
	Designed for their environment, durable low maintenance and safe; meeting relevant market regulations.

Table 4 – Tertiary sector consumer needs

Cryolipolysis Technology trends – Timeline of Technology Development

The Cryolipolysis market is subject to consumer trends driving the development of technology. Cryolipolysis, a consumer health tech trend itself has seen substantial growth in procedure demand. However, as Cryolipolysis technology awareness has increased, so has the rate at which new products and market trends emerge.

The Cryolipolysis procedure was originally developed by Zeltiq Aesthetics; a Silicon Valley healthtech company introducing the procedure CoolSculpting to the global health tech and slimming product market as a non-invasive alternative to Liposuction, receiving FDA approval for procedure and machine in September 2010.

Figure 13 – Image of Zeltiq Coolsculpting Machine and Procedure.

Figure 9 above demonstrates the original CoolSculpting procedure, a clinical appointment in which a technician administers the procedure using a single applicator.

To improve treatment efficiency multiple applicator use was found to be safe, effective and increase revenue leading to the development of "DuelSculpting" a new procedure in which multiple target areas are addressed in a single session.

This market trend encouraged investment into additional Cryolipolysis units to capitalise on the DuelSculpting trends novelty, innovation and therefore consumer marketability.

Figure 14 - DuelSculpting example

Figure 14 presents a standard abdominal DuelSculpting procedure, using two Zeltiq CoolSculpting units simultaneously to address multiple target areas in a single session.

The DuelSculpting trend lead to manufacturers developing units with multiple applicators (figure 6) capable of successfully delivering simultaneous procedures from a single standalone unit, leaving manufacturers of single applicator units at risk of losing market share.

A universal trend observed in cryolipolysis procedure marketing and the subject of many current research studies is the addition of post procedure massage stimulation.

Manufacturers have experimented with post procedure stimulation by incorporating massage functions into the machine applicator, however, there is a current lack of research into the combinations efficacy; presenting the opportunity to research potential benefits of combining Electro Muscle Stimulation with Cryolipolysis.

A further smaller movement in the Cryolipolysis market is the development of compact home use machines, empowering consumers to self-administer treatments on demand.

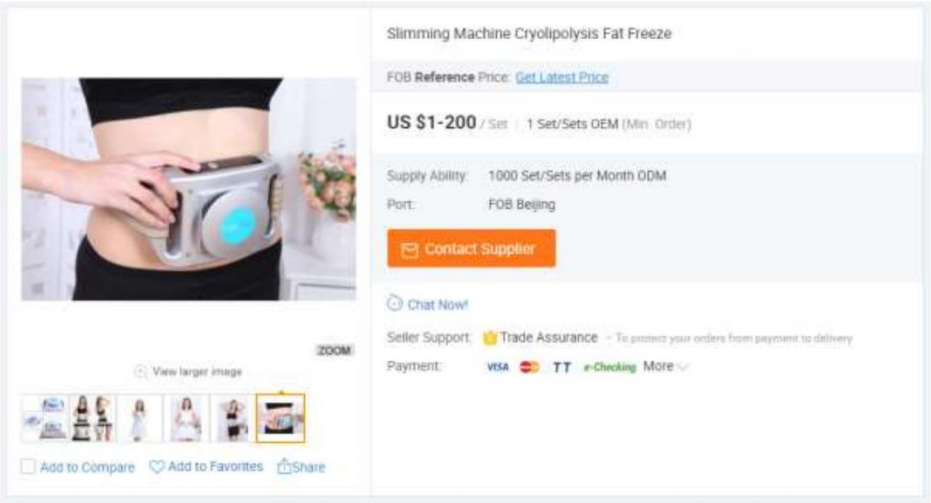

Figure 15 – Personal Consumer Cryolipolysis product Alibaba.

Figure 10, a Cryolipolysis listing from the Alibaba marketplace is an example of a white label home use consumer product available and ready to implement into an existing product line or brand.

The opportunity presented above is ideal for the growing e-commerce market as online entrepreneurs analyse emerging trends to identify new opportunities and “viral” products.

Given the media attention on Cryogenic health and the emerging health tech trend the market may see an influx of independent online retailors shipping low cost off the shelf technology built around online businesses designed for high impact social media target marketing.

Although home use products such as the one featured in figure 4 make up a small percentage of the current Cryogenic health market, personal products may pose a potential threat to the health clinic industry if adoption of the technology becomes mainstream.

Based on the Cryolipolysis trend analysis it’s evident that the markets moving towards smaller, portable and personal Cryolipolysis machines growing alongside the rise of health and beauty apps such as PRIV, allowing consumers to book professional mobile treatments through a mobile or desktop application; presenting potential to innovate within the Cryolipolysis industry by putting in place the technology to enable mobile therapy market to growth.

Cryolipolysis and the media –

Cryolipolysis has been a popular topic of mainstream media interest and discussion. The recent sale of a major industry manufacturer; Zeltiq for $2.48b USD in 2017 has further drawn attention from financial reporters and market analysts.

This section of the report aims to encompass the current state of Cryolipolysis in the media, determining popular areas of interest and concerns.

The following selection of headlines have been taken from both national and international reporting services and further reviewed in a summary of media attitudes.

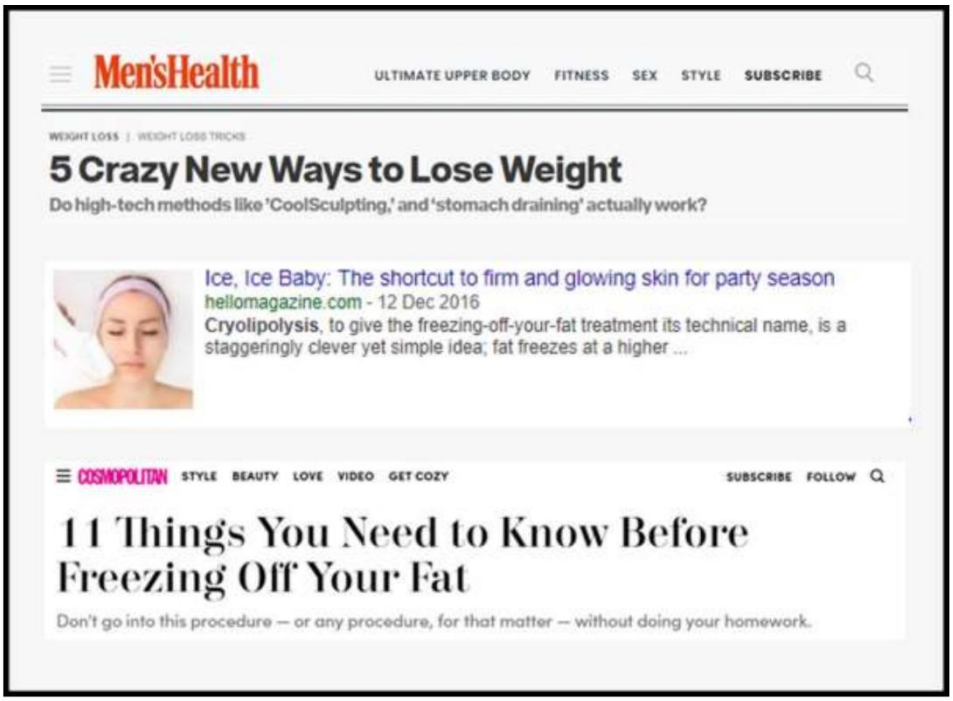

Figure 16 Cryolipolysis Media Board 1 – Media gender differences in Cryolipolysis marketing

Figure 17 Cryolipolysis in the mainstream Media

The headlines above indicate a positive majority attitude towards the Cryolipolysis procedure with the concept of 'freezing fat off" being embraced by reporters, disambiguating the meaning of Cryolipolysis and presenting a simple, effective solution to reducing fat.

Further to this a proportion of headlines returned on a Cryolipolysis key word news search feature notable public figures. Figure 13 includes images of popular British reality television stars undergoing and promoting 'Fat Freeze' procedures, encouraging wider mainstream consumer adoption.

Figure 16 observes gender discrepancies in procedure marketing/reporting with publications boasting a strong male readership such as Men's Health magazine taking a technological viewpoint, emphasising the futuristic high-tech nature of the procedure, whilst publishers with a strong female readership such as Hello magazine opt for a result driven approach to reporting on Cryolipolysis, highlighting the potential outcomes from a body contouring procedure and it's potential to reduce body fat and increase definition.

Although most headlines revolve around the procedures novelty a proportion of publications convey a negative Cryolipolysis attitude exploiting and spinning statistics into shock headlines.

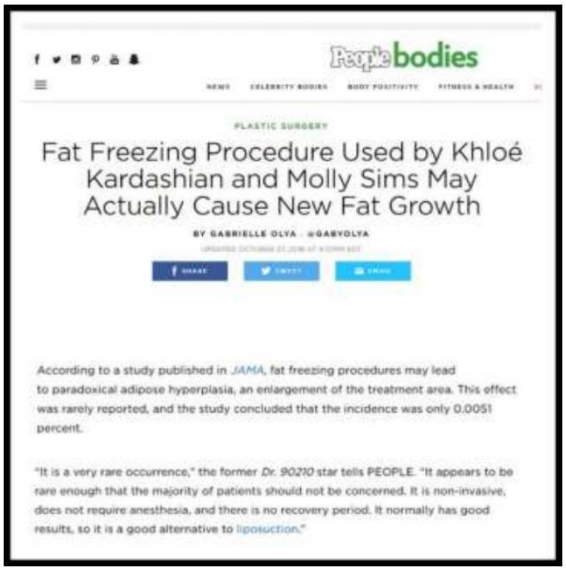

Figure 18 - PEOPLE magazine Cryolipolysis headline

The example above from PEOPLE magazine showcases a 'shock' headline derived from a statistic of 0.0051% of procedures leading to paradoxical adipose hyperplasia or as stated in the headline an increase in fat.

Whilst the procedure is still relatively new to the mass consumer market such headlines could be detrimental to consumer technology adoption and deter future potential consumers.

Figure 19 Daily Mail Online Bizarre safety headline

Figure 15 from the Daily Mail Online plays on the abnormality of the procedure and explores the health, safety and ethical issues around Cryolipolysis. The article undermines the cryolipolysis procedure, with the featured image emphasising it's "bizarreness"

Considering the point above the significance of aesthetics in product development should be noted, inclusively designing products for their environment.

To summarise, the general mainstream media attitude towards Cryolipolysis remains a topic of favourable curiosity with attitudes towards the procedure being generally positive and embracive, however as the novelty becomes exhausted innovation is key to maintaining the interests of consumer and media.

Based on the strength of media interest there is a strong indication of potential to impactfully innovate in the Cryolipolysis marketplace, a topic of emerging popular interest.

Cryolipolysis Business Case Study, Zeltiq Aesthetics -

The following section of this report features a Cryolipolysis business case study discussed as part of a presentation amongst project supervisors reviewing the wider Cryolipolysis market.

The study of Zeltiq Aesthetics was chosen having been the subject of a recent $2.48 Billion dollar acquisition in Feb 2017, the largest Cryolipolysis market announcement to date.

Figure 20 - Zeltiq Case Study Presentation Cover Slide

Figure 21 Zeltiq Case study slide 1

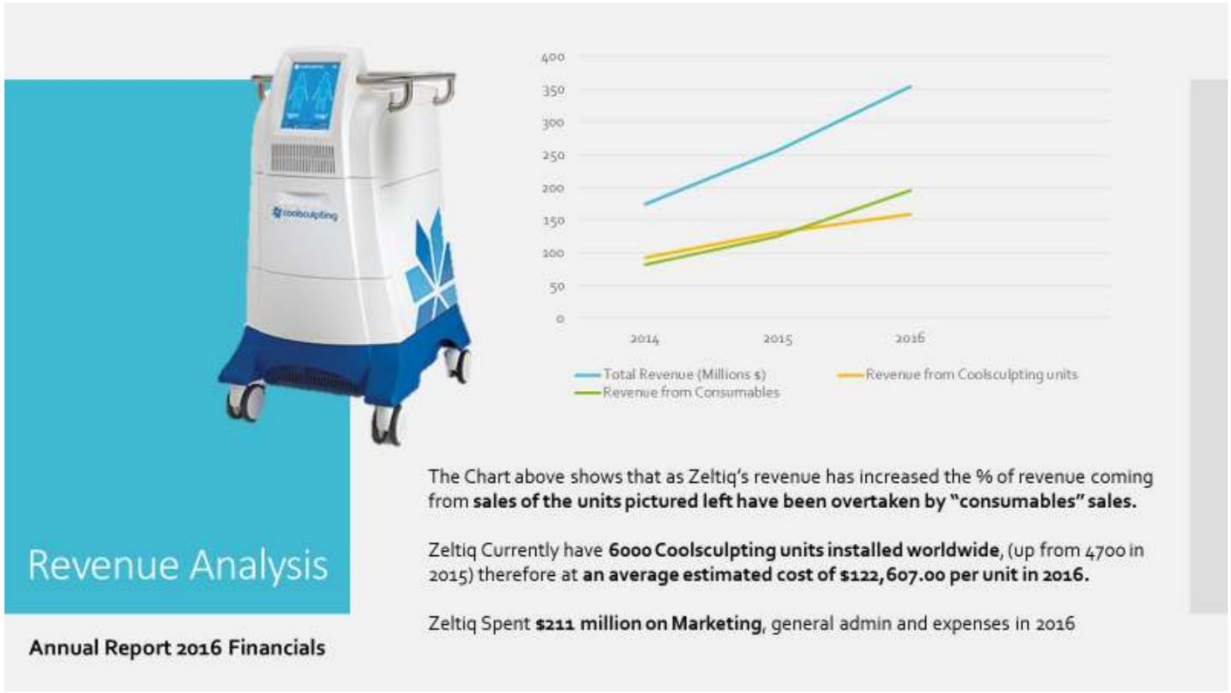

Figure 22 Zeltiq Case study slide 2

Figure 23 Zeltiq Case study slide 3

Figure 24 Zeltiq Case study slide 4

Figure 25 Zeltiq Case study slide 5

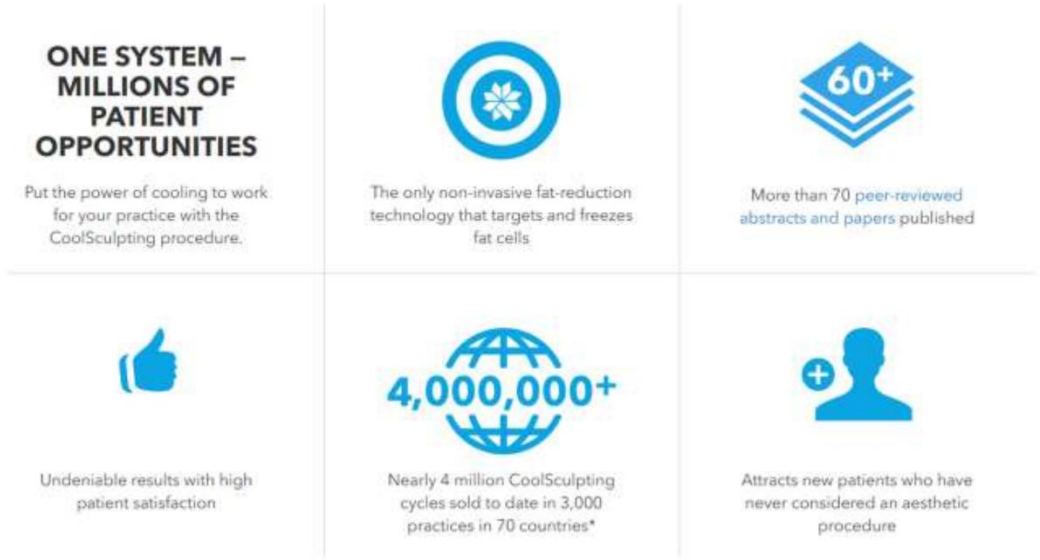

Figure 26 Zeltiq Case study slide 6

Heavily marketed towards health and beauty clinics

Figure 27 Zeltiq Case Study slide 7

Figure 28 Zeltiq Case study slide 8

Zeltiq Case Study Summary

The presentation above explores the drivers behind Zeltiq's success as a manufacturer in the Cryolipolysis market.

The following points highlight key activities evaluated to have significantly impacted Zeltiq's market value and maintained the company as a market leader.

- Pay to play business model – To capitalise on the initial position of introducing a new slimming procedure Zeltiq implemented the CoolCard into CoolSculpting units; requiring an additional non-reusable consumable to be purchased in order to administer a procedure. As competitors have emerged providing alternative Cryolipolysis technology revenues may be subject to decline. Revenues from the sale of CoolSculpting units have been surpassed by consumables revenue.

- In 2016 company reports reveal an annual spending of $211 million on marketing and expenses showing a substantial investment being made into marketing; driving sales of both CoolSculpting units and procedures.

- The company is engaged in ongoing product research and development to supplement existing units; Offering clinics the opportunity to expand the treatments available from their CoolSculpting unit through purchasing additional machine accessories for different target areas, safeguarding the Zeltiq unit against early machine obsolescence.

- Products are developed in line with regulatory standards and accreditment such as the Food and Drug administration (FDA) and the EU CE mark acknowledging health, safety and environmental requirements allowing the free movement of products within the European Market.

- Units are designed for their environment, robust and capable of delivering a high procedure output whilst maintaining a consistency of quality and safety across procedure results.

The points above although observed in the market activity of competiting products outline an approach to new product development assigning product and procedure value through research driven development to establish a successful consumer health product.

Cryolipolysis market summary –

From the research into the industry an overall market summary can be put forth considering the risks and opportunities in the new product development of a Cryolipolysis (slimming) machine.

The research indicates strong Cryolipolysis industry growth to 2024 as analysists claim the technological novelty of the procedure, its rapid non-invasive nature and results driving the procedure demand.

The procedure has received FDA approval with large manufacturers receiving FDA approval for both procedure and technology.

Since introduced, Cryolipolysis technology and procedure has seen limited technological disruption with a large percentage of the market repackaging technology in higher quantities at lower prices, presenting significant potential to explore the opportunities presented from the emerging Health Technology and AI trends to innovate impactfully within the Cryolipolysis market.

The following table categorises and ranks Cryolipolysis market opportunities and risks with a score of 5 presenting the strongest opportunity/most risk to new product development.

Market	Breakdown	Opportunity	Strength
Cryolipol-ysis	**Current Market Climate (Estimate market size)**	Market has seen little disruption since launch through technological innovation. **$4b Dollars PA market**	4
	Future market potential	Market has potential to expand into new segments i.e. portable and personal healthcare	4
	Target consumer	Target consumers Looking for new marketable procedures/investments attracting consumers and increasing potential business revenues.	4
	End user	Strong global market demographic of procedure candidates, looking for quick procedure offering best results.	5
	Market Trends	Emerging mass consumer market trends present opportunity to innovate within the Cryolipolysis market.	5
	Pricing	Procedure pricing offers high revenue potential per treatment timeslot. High value.	5
	Media	Technology still in media interests however beginning to lose its 'novel' headlines.	3
	Marketability	Strong opportunity to market new innovative procedures to a target consumer.	5
Average score			**4.4**
Market	**Breakdown**	**Risks**	**Strength**
Cryolipoly sis	**Technology**	Bringing to market an outdated product, missing emerging trends and not innovating.	3
	Competitors	Competitors developing new technology.	3
	The Media	The media taking a negative interest in the technology and debilitating product adoption.	2
	The Economy	Economic fluctuations leading to a reduction in consumer spending and therefore market strength.	2
Average score			**2.5**

Table 5 - Cryolipolysis market risks and opportunities

The Cryotherapy Treatment Market –

Cryotherapy is concerned with the application of cold, often negative temperatures to relieve injury and improve post training recovery, with some evidence of weight loss. The procedure can be administered either locally using handheld devices or generally known as whole body Cryotherapy chambers/saunas for between two to four minutes at temperatures below -100 °C.

Cryotherapy technology commonly employed by clinics and providers involves the regulated use of liquid nitrogen vapour to rapidly cool preselected areas of the body resulting in reduced inflammation, pain relief and improved muscle recovery.

Figure 29 - Cryo-T Elephant

The example above is of a localised Liquid Nitrogen Cryotherapy unit used in clinics and training facilities. The unit is capable of delivering a stream of cold air to a local treatment area; alternatively, a whole body cryochamber or sauna can be used to administer procedures on a general basis; however whole-body Cryotherapy due to its dissimilar protocols falls outside of the projects scope and thus the report focuses on the localised Cryotherapy technology market.

The combination of Cryotherapy with electro muscle stimulation has been documented in research papers evaluating its efficacy and used in hospitals post-surgery as an anaesthetic with the combination increasing the analgesic effects of Cryotherapy, however the combination is not commercially explored in the therapy and cosmetic market.

Although cryotherapy is highly regarded amongst athletes, coaches and therapists further research has been called for into the procedures efficacy as current data doesn't show significant benefit to the technologies use over ice packs or ice baths and lacks regulatory approval from the FDA.

Cryotherapy market –

The market for Cryotherapy falls within Alternative medicines under the consumer wellness and fitness category. The PwC report "Capture the Growth" referenced in the previous section identifies alternative medicines to be alongside weight loss in terms of market growth with similar figures projected for UK market revenue growth by 2020.

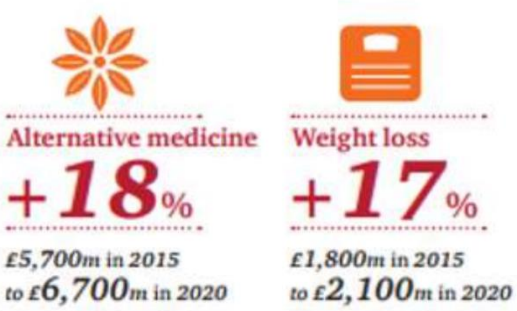

Figure 30 Healthcare spending, capture the growth; the opportunities for new entrants in healthcare and wellbeing, PwC February 2016

Further to this a report published by an independent research group on Medgadget a medical technology website claims the cryotherapy market is expected to grow at a compound annual growth rate (CAGR) of 10% within a 5-year forecast; sharing the adoption of healthcare technology and minimally invasive procedures as a driver behind market growth.

The Global cryotherapy market was valued at $2.5 Billion dollars in 2015 by market researchers Grand View Research, the report further publishes a graph showing projected global cryotherapy market value at a CAGR of 9.7%, in line with the previously projected 10%

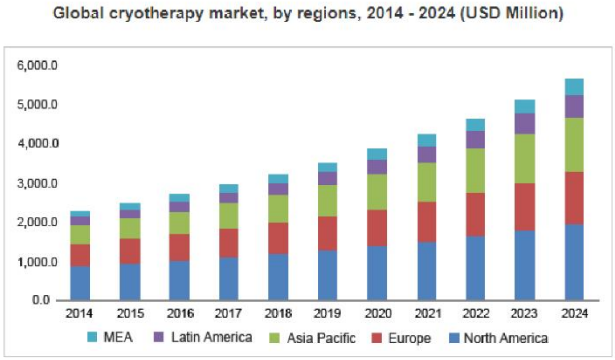

Figure 31 - Global cryotherapy market, by regions - Grand View Research, Cryotherapy Market Analysis October 2016

A further report by BusinessWire on the global Liquid Nitrogen market titled Global Liquid Nitrogen Market 2017-2021 identifies cryotherapy enabling Liquid Nitrogen market growth with analysts forecasting growth at a 5.3% CAGR to 2021.

This increased demand in Liquid Nitrogen may result in demand-pull inflation in which the economy outpaces aggregate supply and resource costs therefore increase, costing more for providers to administer cryotherapy per procedure, however the supply of liquid nitrogen is currently stable.

Research into the Cryotherapy market is limited, however from the current research output there is a strong indication of continued cryotherapy market growth in a 5-year forecast.

Cryotherapy Pricing Review –

The retail price of localised Cryotherapy procedures range between £50 to £150 for a 1hr booking with multiple treatments available including 'Cryo facials' and wellbeing boosting procedures. Additionally, therapists may recommend a course of Cryotherapy treatments dependant on desired outcome e.g. injury rehabilitation with treatment packages priced separately.

Figure 32 Cryoair and Cryoair Mini

No correlation was found between technology brand and procedure pricing evident in the Cryolipolysis market. Prices are relative to the reputation of clinic or treatment provider as opposed to technology manufacturer brand strength assigning value to procedures.

The initial investment into a Localised Cryotherapy unit is conventionally lower than Cryolipolysis machines however, unlike Cryolipolysis, commonly used Cryotherapy devices are dependent on Liquid Nitrogen, C02 (Carbon Dioxide) or other Cryogenic liquid substances and are require manual refilling and maintenance.

An estimation of procedures per Liquid nitrogen tank indicates that a 60L tank could output 100 three minute sessions focusing on a single area or 30 twelve minute procedures addressing multiple areas of the body.

The table below reviews the price of local Cryotherapy units.

Market Leaders	Unit cost (approx. £GBP)
Cryo Science Cryo Penguin	£14,000
KRIOSAN	£17,000
Metrum Cryflex CRYO-T elephant	£6,300
Gymna Cryoflow 1000	£7,000

Table 6 Cryotherapy unit prices

Given the lower unit prices of Local Cryotherapy machines the competition from value replications has less impact on the market. This is reflected in the lack of replicated Local Cryotherapy units available on global manufacturing trade platforms such as Alibaba.

Consumer Profiles: The target consumer –

The market for cryotherapy is growing alongside the adoption of technology from Athletes, clubs and training professionals, translating into mainstream consumer attention as a means of improving physical training recovery and wellbeing.

The market for sports injury and recovery related local cryotherapy is predominantly male however the versatility of the treatment enables procedures such as cryo-facials and cellulite reduction, popular in the cosmetic, health and wellbeing market to be performed from the same machine; Highlighting gender neutrality as a point of significance to machine design.

The following consumer profiling analyses the Localised Cryotherapy target consumer.

Profile Category	Profile Group	Target Procedure Consumer
Cryotherapy Demographics	Age	18 to 55
	Gender	Neutral
	Income	High income £40k+
	Culture	Western Culture, Sports, fitness, image, wellbeing, health
	Family Cycle	Single or married possibly with Children.
	Work	Athletics, Media, Business, personal relation, sports industry, city, office, travel, professional, no work.
	Education	Higher education, secondary school, College, University.

Profile Category	Profile Group	Target Procedure Consumer
Cryotherapy Psychographics	Lifestyle	Health and fitness, athletic, Social, Working Professional, digitally active, media conscious, following new trends and news.
	Concerns	Concerned with health, fitness wellbeing, self-esteem, time, positivity, aging, image.

	Opinions, Attitudes, Interests and Hobbies	Goal driven, motivated, interested in the best new procedures, efficiency, open to experience, media engaged, new trends, News, health, wellbeing and fitness blogs, personal treatment.
	Degree of Loyalty	Brand loyal, quality/image over value, Lifestyle brands, willing to try new trending products.
	Occasions to undergo a procedure	Post Training, increased recovery, injuries, experience purchases, self- reward, to relax.

Table 7 Consumer profile Cryotherapy

Consumer demographics points of interest –

The Cryotherapy consumer differs from the previously reviewed Cryolipolysis consumer as Cryolipolysis is exclusively intended for the destruction of fat, whilst cryotherapy explores the application of Cryo technology in health and wellbeing.

Therefore, the prior highlighted shift in consumer attitudes embracing health and fitness as part of lifestyle may increase consumer curiosity in procedures such as Cryotherapy to supplement training, however due to cost regular treatments such as Liquid Nitrogen cryotherapy remain most accessible and beneficial to high performance athletes.

A higher earning consumer was thus identified, conscious about health and looking for the best products on the market to benefit their health and wellbeing, sharing similar attributes with the Cryolipolysis consumer in terms of image awareness.

Given the nature of cryotherapy as a resource to professional athletes the demography of the target consumer is much broader, encompassing high performance athletes globally. However, the use of Local Cryotherapy cosmetically or for wellbeing shares the geographical location with Cryolipolysis consumers; affluent regions with the availability of disposable income.

The Cryotherapy Technology consumer: Clinics, sporting facilities and treatment providers

The technology consumer market is composed of a range of cosmetic and sports industries with target consumers including health clinics, sports and training facilities (including high end gyms) physiotherapists and specialised cryotherapy clinics.

In the interests of technology consumers are: emerging trends, product marketability and added value at offering strong earnings potential.

The following table outlines the needs of technology consumers, from new product development.

Consumer	Product needs
Tertiary Sector Cryotherapy - (clinics, health and wellbeing centres, Gyms, Spas, clubs)	Offer significant innovation or marketability to compete with existing technology.
	Present value as an investment capable of increasing revenues; contributing to business growth.
	Backed by research and development increasing consumer confidence and procedure marketability therefore adoption.
	Developed alongside emerging social trends, encompassing the market direction and consumer attitudes to deliver disruptive products and present potential for future market growth.
	Efficient
	Designed for their environment, durable low maintenance and safe; meeting relevant market regulations.

Table 8 Cryotherapy Technology consumer needs Tertiary sector

Cryotherapy Technology trends

The Cryotherapy market is influenced by consumer trends and attitudes driving the development of new Technology, most predominantly the emerging health and fitness culture amongst the demographic of 18+ consumers presents significant potential for mainstream standardisation of cryotherapy technology as a health and training resource.

The price of clinical Cryotherapy procedures however, restricts the technologies use to top athletes and high earning health conscious consumers, therefore the market is seeing a rise in lower cost alternative Cryotherapy technology exploiting the shared biomechanics behind high end procedures to target the mass market consumer, capitalising on Cryotherapy technologies heightened state of public interest.

Figure 33 Aircast Knee Cryo/Cuff with cooler, RRP £98.79

Above is a readily available consumer Cryotherapy product; designed for home use injury rehabilitation and improved post training recovery, presenting a mid-range mass market alternative to clinical high cost Cryotherapy.

The home use product trend apparent across the Cryotherapy market is reflected throughout product types and price ranges as a growing number of top athletes are reportedly installing whole-body Cryotherapy chambers in their home to use as and when required.

Ice cool Ronaldo: Real Madrid star buys -160C Cryotherapy chamber for his house

By PETE JENSON FOR MAILONLINE

Figure 34 - Mail Online, Cristiano Ronaldo buys Cryotherapy chamber

The article from the headline above states that €45,000 was spent installing a whole-body Cryotherapy chamber in an athlete's home having first tested Cryotherapy at a local gym. Although indicative of a trend within the separate whole-body cryotherapy market, a growing number of top athletes have followed with home technology integration highlighting positive attitudes towards home use healthcare and wellbeing products, ideologies transferrable to the local cryotherapy market.

The versatility of Cryotherapy technology has enabled clinics to experiment and develop new procedures to maximise the efficiency and revenue potential from a single unit, ranging from conventional injury and pain relief procedures to anti-ageing cryo-facials.

Figure 35 - Example Cryo Facial procedure

Figure 35 displays a machine normatively used as an aid in local injury relief delivering a cosmetic anti-aging cryo facial procedure. The multipurposed technology nature is relatively niche in healthcare however as software is increasingly defining the parameters of technology multipurpose machines could emerge as a popular trend in the clinical industry, delivering various procedures from a single unit, increasing revenue potential.

Cryotherapy and the media –

The topic of Cryotherapy has been of growing popular interest in the media with the widespread adoption of the technology amongst sporting professionals drawing a wider public audience.

The following section of the report aims to encompass the current state of Cryotherapy in the media, determining popular areas of interest and concerns.

The selection of headlines below have been taken from both national and international reporting services and further reviewed in a summary of media attitudes.

Figure 36 Review of Media attitudes towards cryotherapy

A Cryotherapy key word google news search returns predominantly whole-body cryotherapy headlines focused on the adoption of technology by sporting professionals and celebrities with articles looking into the procedures efficacy and results.

It's evident that Cryotherapy reporting is driven by procedure novelty and therefore subject to intense periods of heightened media interest followed by a relative decline in interest, evident in Cryolipolysis, Cryotherapy and the launch of new products to market.

Local Cryotherapy currently has minimal presence in the media with whole-body cryotherapy taking prevalence, however an impactful point of discussion influencing consumer attitudes towards the overall Cryotherapy technology market is it's efficacy over traditional ice baths and ice packing treatments.

'It's smoke and mirrors': Arsène Wenger takes aim at cryotherapy

- Arsenal face three games in seven days, including Belarus trip
- 'The ones who prove it works are paid by the guy who says it does'

Alexis Sánchez is likely to play twice in the Premier League this week but to miss the Europa League trip to Belarus. Photograph: Stuart MacFarlane/Arsenal FC via Getty Images

Arsène Wenger has questioned whether modern recovery treatments for players such as cryotherapy actually work and wonders if they have been pushed by specialists with vested interests,

Figure 37 the guardian - Smoke and mirrors

The headline above exemplifies this statement highlighting the statements put forth by a leading sports coach. Raising the concern that Cryotherapy may be "pushed by specialists with vested interests"

Further research into Cryotherapy business reporting returns a supporting article suggesting collaboration between technology manufacturer and Liquid Nitrogen suppliers.

Figure 38 Air Liquide UK partners with Impact Cryotherapy

In addition to the points identified above the argument presenting most weight against Cryotherapy is the lack of FDA approval exploited in figure 39 below. To summarise given enabled consumers accessibility to research procedures, the portrayal of Cryotherapy in the media may deter consumers from embracing Cryotherapy.

Figure 39 - Elle magazine and the FDA

Cryotherapy market summary –

There is indication from the research of overall Cryotherapy market growth, driven by the adoption and exposure of whole-body Cryotherapy as a resource to Athletes and sporting professionals.

The use of technologically enabled cryotherapy devices such as Liquid Nitrogen cooling units has not been granted approval from regulatory bodies such as the FDA posing a risk to the market through reduced mass market consumer confidence.

The local Cryotherapy market however is under pressure from alternative cryotherapy home use products sharing similar results with more expensive Cryotherapy treatment procedures.

The following table categorises and ranks local Cryotherapy market opportunities and risks with a score of 5 presenting the strongest opportunity/risk to new product development.

Market	Breakdown	Opportunity	Strength
Cryotherapy Local	**Current Market Climate (Estimate market size)**	Market has seen little disruption due to innovation. Stagnating $2.5b Dollars PA Market	3
	Future market potential	There is indication of continued market growth.	3
	Target consumer	Target consumers Looking for new marketable procedures/investments attracting consumers and increasing potential business revenues.	4
	End user	There is a global market of procedure candidates, including Athletes and wellness conscious consumers using the technology actively.	3
	Market Trends	Market trends are restricted by the Technology, however strong trends are present and emerging in technology enabled fitness and recovery.	3
	Pricing	Procedure pricing offers high revenue potential per treatment timeslot. High value. But uses consumables (LN2)	4
	Media	Local Cryotherapy has limited exposure compared to WBC however is still a niche within a popular topic.	3
	Marketability	Potential to market a novel procedure to the consumer market.	5
Average score			**3.5**
Market	**Breakdown**	**Risks**	**Strength**
Cryotherapy	**Technology**	Bringing to market an outdated product, missing emerging trends and not innovating.	2
	Competitors	Competitors developing new technology.	3
	The Media	The media taking a negative interest in the technology and limiting product adoption.	4
	The Economy	Economic fluctuations leading to a reduction in consumer spending and therefore market strength.	2
Average score			**2.75**

Table 9 - Cryotherapy market opportunities and risks

III – Market Report Conclusions

The following section of the report comparatively reviews both Cryotherapy and Cryolipolysis markets identifying areas promising most market opportunity for future innovation in the development of a combined Cryo-EMS prototype.

This section of the document further aims to help outline a strategic product proposal and development plan for impactful Cryogenic market innovation.

The table below compares previously reviewed market rankings offering a score based metric of comparison.

Market Segment	Cryotherapy Opportunity Ranking	Cryolipolysis Opportunity Ranking
Current Market Climate	3	4
Future Market Potential	3	4
Target Consumer	4	4
End User	3	5
Market Trends	3	5
Pricing	4	5
Media	3	3
Marketability	5	5
Average Market Score	**3.62**	**4.4**

Table 10 A comparison of market opportunity strengths

The table outlines a stronger average Cryolipolysis market opportunity based on the exploration of market segments, presenting ample potential to introduce a Combined Cryo-EMS procedure exploiting the combinations physiological benefits to improve procedure efficacy and impactfully innovate within the existing Cryolipolysis market.

A further assessment of risks to new product development was performed to be considered in the proposal of a new product.

Market Risks	Cryotherapy Risk Ranking	Cryolipolysis Risk Ranking
Technology	2	3
Competitors	3	3
The Media	4	2
The economy	2	2
Average Risk Score	**2.75**	**2.5**

Table 11 Cryotherapy Cryolipolysis Risk comparison

From this comparative table it's evident that Cryotherapy poses a higher average risk factor to the development and introduction of a new Cryo-health product, limiting the market potential of a Combined procedure.

Project Cryostim

Table of literature

Ricardo Real (MscRes Engineering)

A categoric database of the literature read in relation to the Cryostim project. The literature falls into multiple disciplines and has subsequently been categorised into the relative subject areas. To distinguish between disciplines and facilitate data access, category codes were devised along with a universal literature entry table shown in the example below.

Literature Category Codes

- **Cryobiology**	**Cryob**
- **Electro Muscle Stimulation** Physiology	**EMSP**
- **Human Physiology and Anatomy**	**HPA**
- **Cryogenics and refrigeration** Technology	**CryoT**
- **Electro Muscle Stimulation** Technology	**EMST**
- **New Product Development**	**NPD**
- Electronics	
- Standards	
- Design/Design Engineering	
- Patents	
- **Project Management**	**PM**

Literature Entry Table – A table composed of a range of fields designed to summarise key information and allowing for elaboration in areas of interest.

Title:	**Date**:
Author:	**Category**:
Summary:	
Findings:	
Areas for further research:	
Summary Points of Interest:	

The entries to this database are in Chronological order throughout projects natural development

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Title: In Introduction to Human Anatomy	**Date**: 1981
Author: J.H. Green P.H.S. Silver – Oxford Medical Publications	**Category**: HPA Book
Summary: An introduction to the structures of the living human body.	

Findings: Some topics in this book were found to be of significant relevance to the Cryostim project in developing an understanding of the mechanics of Cryo treatment and the bodies autonomous reaction to the stressors imposed by Cryotherapy, raising some interesting questions and topics to be further explored.

The areas of the human anatomy found to relate to the project can be divided into the following systems and structures, The Nervous System, Blood Vessels, the Lymphatic system and the Epithelium/Connective tissue.

The Central Nervous System (CNS) – The peripheral nervous system is made up of neurones; sensory neurones which send information (nerve impulses) from sensory receptors to the CNS and Motor neurones sending information away from the CNS to effectors (muscles and glands).
-The CNS consists of two systems, the Autonomic nervous system (ANS) regulating visceral structures, ultimately controlled by the hypothalamus and Vasomotor centre and secondly the Somatic Nervous system controlling skeletal movement and muscles.
- The CNS reacts to stimulus such as touch and temperature by sending nerve impulses to the brain which responds accordingly triggering a sympathetic or parasympathetic reaction.

Given the exposure to both cold temperature and electro stimulation throughout treatment a further analysis of the CNS's autonomic response to these stimuli should be further researched and considered.

Blood Vessels - A Blood vessel is a tubular structure carrying blood through tissues and organs including Arteries (carrying Oxygen rich blood from the heart) Veins (carrying blood back to the heart) and capillaries (connected to both arteries and veins feeding oxygen and nutrients to other tissue in the body)

- Connecting Arteries and Capillaries are Arterioles, the Arteriole controls the blood supply to the capillaries and is innervated by the sympathetic nervous system (by factors such as hot/cold) opening to increase blood flow or contracting to reduce flow to the capillaries, the arterioles also play a key part in maintaining blood pressure.

- Capillaries are where nutrients and oxygen are delivered to tissue, they are thin walled and only allow blood cells to go through one at a time. No muscle in capillaries or nerve connections however can contract and completely obstruct the flow of blood. They are sensitive to local factors, and worth further researching. Accumulation of waste products in tissue causes relaxation of cells allowing blood to flow freely. (to take with it some of the waste products?)

- Veins, with blood having seeped through the capillary bed it's returned to the heart via venules and veins. When muscles contract, they squeeze veins and valves along the vein prevent backflow of blood, when muscles relax that segment of vein fills AKA Muscle pump. Important note muscle pump requires alternate contraction and relaxation of muscles.

Lymphatic System – The lymphatic system deals with tissue fluids (interstitial fluid derived from blood in capillaries) which has seeped into the tissue spaces (gaps between cells)
-Capillary walls are impermeable to plasma proteins and tissue fluid therefore has lower protein concentration than blood.
- At the arterial ends fluid is forced out of capillaries into tissue spaces by the blood pressure, at the venous ends fluids are returned to the capillaries by osmotic forces and difference in plasma protein concentration. As plasma protein increases in the venous ends osmotic forces further increased and pressure in the arterial end reduced (a pumping system of sorts)
- Blood pressure falls as blood passes from Arterial to Venous ends of capillaries.
- It is only possible for the return of fluid at venous ends to exceed what passes out at the arterial end on short term basis and leads to a reduction in interstitial fluid and increase in the volume as fluid returns to blood (restoring plasma volume). In the opposite situation, where the fluid is reabsorbed slower this leads to oedema a swelling of the tissue spaces.
- The lymphatic system also deals with the issue of removing leaked plasma protein and other cellular material which cannot pass through the capillary walls, such cellular material is osmotically active and reduces the return of fluid into the bloodstream resulting in oedema.
- The Lymphatic system acts as a mechanism to ensure the escape of surplus tissue fluid and return leaked protein plasma, it does so with lymphatic capillaries (which unlike blood capillaries cellular debris and plasma protein can readily enter) these lymphatic capillaries join to make larger lymphatic vessels, containing valves to ensure lymph doesn't go back to tissue fluid.
- The Lymphatic system plays a key role in the absorption of fat during fat absorption the lymph contains so many fat droplets it looks like milk (what happens to the fat? And how does the fat end up in the lymph?)
- Lymph nodes have a reticulum (net) structure which traps cellular debris which is then processed and destroyed by phagocytes.

Epithelium and connective tissue – Every cell in the body is either Epithelium or connective tissue, Epithelium lines surfaces on the outside or the inside of the body and connective tissue are structures such as bone, cartilage muscle etc. as a rule of thumb connective tissue are structures which won't have contact with the outside world, in any way.
- Skin, the skin is the largest organ in the human body covering approx. 1.75sq m. The skin is made up of two layers, the dermis a vascular connective tissue and the epidermis, the outside skin.
- the dermis has an extensive sensory nerve supply as well as a motor supply regulating flow of blood in skin controlling body temperature momentarily.
- The skin is the organ by which body temperature is controlled, like a radiator blood flow to the skin is increased raising skin temperature, and cooled further by sweating.
- Skin Blood Flow is ultimately controlled by the heat regulating sensors in the brain and the calibre of blood vessels in the dermis such as arterioles, capillaries ect regulated by nerve impulses for stimuli such at touch or temperature.
- Cutaneous nerves, the skin is richly innervated with sensory nerves forming part of the peripheral nervous system.

Fascia – Just below the dermis is the superficial fascia a loosely arranged meshwork filled with fat. These layers are of importance in determining the body surfaces contours.

- Fat conducts heat very slowly and is important in determining the heat loss rate in adverse conditions.

Conclusion - The notes above conclude the findings and points of interest derived from the introductory human anatomy text, and the most important piece of information to take from said text is the idea that everything is connected, a system in which to understand must be considered as a whole, as a chain reaction employing multiple responses, and you need a depth of understanding composed from a range of research to explore the conditions in order to design around unwanted reactions.

Further research should be done into responses to certain stimulation I.e. temperature and electro stimulation, as well as begin to consider and analyse medical devices already employed to create desired conditions.

Areas for further research:
Central nervous system –
How does the CNS react to cold stimulus?
Role of visual stimulus on Autonomic nervous system? (possible placebo reaction?)
Does electro stimulation trigger a response from the CNS ANS?
Blood Vessels –
What happens to the Arterioles in cold exposure and electro stimulated?
Which stimuli do capillary beds react to?
Lymphatic System –
How does fat get absorbed into the Lymphatic system and what happens to it?
Research into cryotherapy and electro stimulation on the Lymphatic system?
Epithelium and connective tissue –
Research the possible effects of over exposing the skin to low temperature

Summary Points of Interest: All points in the areas to further research

Title: Autonomic nervous function during whole body-body cold exposure before and after cold acclimation	**Date**: 09/2008
Author: Tiina M. Makinen, Matti Mantysaari, Tiina Paakkonen, Jari Jokelainen, Lawrence A. Palinkas, Juhani Hassi, Juhani Leppaluoto, Kari Tahvanainen, and Hannu Rintamaki	**Category**: HPA Research Article

Summary: A paper found of interest on the function of the autonomic nervous system when exposed to cryo conditions also further exploring the idea of cold habituation to determine the autonomic response to cold exposure over a prolonged period of treatment.

This paper provided some critical insights and answers to questions raised in the Human Anatomy ANS chapter on the kind of reaction triggered by cold exposure, sympathetic or parasympathetic.

Findings: The experiment examined 10 male participants exposed to a control temperature of 25°C and a cold environment of 10°C for 2 hours on 10 successive days in a laboratory with heart rate and blood pressure recorded during an isometric handgrip test at the beginning and end of cold acclimation.

The research concluded that acclimation resulted in a reduced plasma norepinephrine levels meaning that the nervous systems response is parasympathetic as opposed to sympathetic, resulting in reduced blood pressure, and increased blood flow in vessels, open arteriole and pressurised capillaries, as well as a slightly reduced heart rate in BPM. Although the research also suggested that initial cold exposure increased sympathetic activity, and interesting point to consider when proposing a recommended length of treatment is does everyone become acclimated to cold exposure at the same rate and do these results transfer to participants with larger amounts of superficial fascia? (fat) thus Blood in the tissue/capillaries would have to be measured to determine blood pressure and diagnose the response as sympathetic or parasympathetic. This also raises the question of to what temperature should the skin be cooled in localised treatment and for how long. To determine this further research into the physiology and Cryolipolysis.
Areas for further research: -Differences in human anatomy and the potential for personalised treatment. -How is the body response monitored to ensure optimal treatment? (links back to top question) -Cryolipolysis introduction to, and physiology. -How long does cold acclimation last and take to develop? Which factors determine differences.
Summary Points of Interest:

Title: Turning down heating can beat diabetes	**Date**: 27/04/2017
Author: Giles Sheldrick – The Daily express	**Category**: HPA Tabloid paper
Summary: A headline newspaper article on the health benefits of living in the cold, "Turning down heating can beat Diabetes"	
Findings: Firstly, from an economic point of view a paper publishing a headline front Page story on the health benefits of reducing heating shows promise of a potential developing mainstream acceptance of cryo treatments for a much broader range of conditions, edging away from the futuristic pseudoscience label treatments have been previously put into and changing public conception through the publication of research in printed tabloid literature. A promising step. Secondly the article itself goes onto briefly explain the points made on the front page and claims that temporary exposure to cold conditions increases metabolism and energy expenditure and therefore could slash obesity rates. It also states that this research indicates mild cold and variable temperatures may benefit our health and the society needs to redefine its idea of thermal comfort. The link researchers found to helping 'beat diabetes' comes from the observation that the cold stimulates the metabolism as the body must work to maintain a core body temperature (homeostasis) and thus consuming glucose in the blood. It could be argued that this would only be temporary as the body would eventually become acclimated to the cold exposure.	
Areas for further research: Effects of cryo treatments on metabolism Further mainstream publications on cryo treatments	

Summary Points of Interest:	
Title: Introduction to Human Anatomy and Physiology	**Date**: 1992
Author: Eldra Pearl Soloman	**Category**: HPA Book

Summary: An introduction to the Human Anatomy and Physiology, a book looking at both structures and functions of the human body.

Findings: The anatomy and physiology of the human body are closely related, expanding on conclusions drawn from a previous book on human anatomy, this text explores its relation to human physiology and introduces new topics and ideas relevant to the Cryostim project.

The following topics were found to contribute additional information to the processes engaged in cryo conditions, including the Metabolism, the muscular system, sense organs, the endocrine system.

The Metabolism – The Metabolism can be broken down into two parts, Catabolism and Anabolism, with the Anabolic process being the breaking down of nutrients to create raw materials used to manufacture chemical substances and body parts, and Catabolism the process of metabolising for sustaining body function, sending nerve signals ect.

Metabolic activity is continuous and so the body must be carefully regulated to maintain a constant internal environment, therefore under external influencers such as cold exposure and ems the body must increase its metabolic activity to maintain homeostasis, generating energy through the metabolic system to sustain the increased demand on the body.

The Muscular System – The action of muscles is key to sustaining a constant physiological state, it is fundamental in the return of blood to the heart and in executing everyday movements. Furthermore, an understanding of the muscular system on a physiological and anatomical level is of relevance to the development of the Cryostim project when considering the combination of cryocooling with electro muscle stimulation and the possible benefits of doing so.

The basics of the muscular system, each skeletal muscle is an organ and has its own nerve supply accompanied by a system of blood vessels that supply nutrients and oxygen and carry out waste. Each muscle is made up of multiple muscle fibres in bundles known as fascicle with muscle fibres connected to nerves through neuromuscular junctions (motor end plates). A further analysis of the anatomy of muscles would be of importance in isolating key muscle areas for EMS and localised Cryostim treatments.

Where do muscles get energy from? The immediate source of energy for muscles is drawn from the energy molecule ATP (Adenosine Triphosphate) however this is shortly depleted after a few seconds of activity therefore the muscle cell has a backup store of Creatine Phosphate. Creatine phosphate can be stock piled and transformed to ATP upon request however the energy source will also drain and require replenishment. The energy for making Creatine phosphate comes from fuel molecules glucose, stored in muscle cells in the form of glycogen. As required Glycogen is metabolically degraded to yielding glucose through cell respiration thus a question that arises is would the combination of Cryocooling with EMS result in a faster depletion of energy stores, especially during the cold acclimation process where the metabolism would be further stressed with a sympathetic response to maintain homeostasis in cold? Further to this does the type of

muscle contraction effect the rate of energy depletion, and which type of muscle contraction is EMS, Isotonic (moving) or isometric (resistance)?

The Sense Organs – The skin is filled with tactile receptors, which respond to pressure touch and sensation, therefore further research is required on how the body responds to touch and sensation as the administration of the treatment could be touch based or is there research to suggest non-touching treatments are beneficial? Also, does the nervous system have a hierarchy system? If two sensory stimuli are simultaneously innervating the nervous system does one have priority?

The Endocrine System – The endocrine system works with the central nervous system to maintain the steady state of the body; it plays a key role in sustaining homeostasis. One function of the endocrine system which may be very relevant to the project is the regulation of glucose in the blood using insulin, (insulins main action is to stimulate storage of glucose, stimulating cells to take up glucose from blood) could glucose blood levels be regulated by cryostimulation by using glucose in blood instead of storing it? Relating back to the newspaper article.

Provided the conditions are adequate for cell respiration ATP (adenosine triphosphate) can be converted directly from glucose to energise muscle, and as the stimulation doesn't involve strenuous exercise oxygen supply could also be appropriate for cell respiration to create enough ATP to energise muscle to absorb glucose in body.

Areas for further research:
-Studies on the reaction of the metabolism in cold environments
-Would the combination of Cryocooling with EMS deplete energy stores at a faster pace? Meaning possibly shorter sessions to avoid exhaustion, at least during the period of cold acclimation.
-What type of muscle contraction is EMS? Isotonic and isometric and the effects of cold exposure to the muscle under contraction
-Hierarchy of the nervous system, what happens if two stimuli are simultaneously innervating?
-Regulation of Glucose in the blood and how EMS + Cryo can help

Summary Points of Interest: all

Title: Human Physiology the basis of medicine	**Date**: 2006
Author: Gillian Pocock, Christopher D. Richards – Oxford University Press	**Category**: HPA

Summary: A concise textbook of physiology covering all aspects of a preclinical course in physiology, the textbook is primarily for students of medicine therefore clinical implications of the subject are deliberately emphasised.

An area which this text explores that hasn't been covered by other introductory texts is Lipolysis, a fundamental to understanding the basic fat destroying process of cryotherapy and a precursor to Cryolipolysis.

Findings:

Lipolysis – The process of lipolysis is a result of stimulation of the sympathetic nervous system and subsequent release of epinephrine and catecholamine's, the epinephrine stimulates vasodilation

in muscles and bronchodilation along with an increase in heart rate, however the catecholamine exerts a very potent lipolytic action in adipose (fat) tissue, stimulating lipases to break down fats to liberate free fatty acids and glycerol, however as a direct result this also increases plasma glucose levels. Lipolysis through this process could be more effective in whole body cryotherapy and longer/more frequent sessions as this process would presumably take longer than cryolipolysis, however standard lipolysis would still be present in a cryolipolysis treatment.
Areas for further research: - Background effects of Lipolysis during Cryolipolysis - Cryolipolysis
Summary Points of Interest:

Title: Cryotherapy	**Date**: No Date
Author: Not published	**Category**: CryoB
Summary: An overview paper on cryotherapy and its applications to treatments of Anaesthesia, Hypertonicity, Inflammation, swelling control.	
Findings: <u>Introduction</u> - Cryotherapy has been historically used to provide pain relief, reduce fever, slow the damage of thermal burns, control bleeding and prevent or reduce Oedema caused by tissue trauma. An interesting note from the paper is an insight into the factors governing the rate of cooling body tissue, firstly the cooling effect will decrease as the depth of tissue increases and secondly the time required for cooling to be effective is will vary according to the type of tissue being cooled. The speed of cooling increases as fat decreases. This paper also explores the concept of slowing of the amplitude and frequency of motor end plate potentials and increases in their duration, concluding that if cooling drops below 5°C at the neuromuscular junction blockage of the junction has been shown to occur. Furthermore, the sensory nerves in the skin are provoked to fire continuously until physiologically exhausted causing temporary anaesthesia.	
Areas for further research: - How can the cooling be measured constantly in variable depths of adipose tissue?	
Summary Points of Interest:	

Title: Cryotherapy: overview, mechanism of action, Treatment Modalities using cryotherapy	**Date**: 29/03/2017
Author: Jacob G Unger, MD; Chief editor: Dirk M Elston	**Category**: CryoB
Summary:	

An overview of cryotherapy in cryosurgical applications as a commonly used in house treatment of a variety of benign and malignant lesions. This paper serves as an introduction to the topic of cryosurgery and its treatment of medical conditions. Although of distant relation to the Cryostim project.
Findings: Points of interest – Although this paper is of little relation to the proposed applications of the Cryostim project it brings up some points of interest from surgical cryotherapy. One note is the on the topic of using disposable attachments over non-disposable attachments in parts in contact with the skin due to HIV and other communicable diseases, therefore disposability is a convenient and simple solution to the problem on contamination. Furthermore, it is noted that Adenovirus is capable of survival in liquid nitrogen therefore the same source of liquid nitrogen should not be used with different patients. Finally, the topic of Cryolipolysis is mentioned briefly in the back of the paper however doesn't elaborate more than stating its novelty and recent FDA approval.
Areas for further research: -Health and safety in relation to the project, transcutaneous contact in particular -Cryolipolysis
Summary Points of Interest:

Title: Cryolipolysis for subcutaneous fat layer reduction	**Date**: 2009
Author: Mathew M. Avram, Rosemary S. Harry	**Category**: CryoB
Summary: A study reviewing the efficacy and safety of cryolipolysis for localised fat layer reduction with an analysis of methods employed in localised cooling. The paper explores a range of papers drawing conclusions from both animal and human studies.	
Findings: Cryolipolysis is becoming a popular alternative to other fat reduction procedures such as liposuction due to being non-invasive and offering a reduced risk profile, although less effective cryolipolysis has proved efficient in the reduction of localised fat cells without damage to surrounding tissue. <u>Background</u> – Case reports were initially observed in infants describing clinically evident inflammation after exposure to an ice cube for a few minutes. It was observed that minor exposure of cold demonstrated a perivascular infiltration of Histiocytes and Lymphocytes extending into the dermis and subcutaneous fat approximately 24 hours after the initial cold exposure, the change become more evident 72 hours' post exposure with additional inflammatory cells appearing in the subcutaneous fat layer. Slight inflammatory progression continued for three more days with an increase of histiocytes, neutrophils, lymphocytes and other mononuclear cells surrounding adipose tissue. Within a few weeks the cold panniculitis resolved itself with no damage to surround tissue and no evidence of cryoglobulins <u>Pre-clinical studies</u> – Manstein et al performed animal experiments to evaluate the potential of achieving selective damage to subcutaneous fat with controlled application of cold to skin. The	

study consisted of three separate experiments, an exploratory study, a dosimetry study and finally a health and safety study, the cooling applied was kept relatively consistent throughout at temperatures between -1 and -8 for a range of time periods from 5 to 21 minutes. The tests used a mix of cooling technology with the first using a plate cooled by circulating antifreeze solution and the following tests a thermoelectric cooling element, however cooling was transferred in all cases by a flat plate.

All experiments observed a similar reduction in the superficial fat layer with no apparent injury documented in any of the test sites successfully demonstrating it was possible to "non-invasively induce selective, localized damage to subcutaneous fat without injury." Mansteins experiments were further supported by other animal studies however these further explored the combination of cryocooling with post cooling five-minute period of tissue massage it was documented that "treatments resulted in a significant reduction in the superficial fat layer" but doesn't elaborate on if the period of tissue stimulation benefitted the treatment in terms cell destruction, again no signs of damage to tissue were apparent.

Observed mechanisms of action Cryolipolysis – Histologic analysis at different time periods concluded that cryolipolysis causes the death of adipocytes that are subsequently engulfed and digested by macrophages. Immediately after treatment there is no changes in subcutaneous fat however within three days there is evidence of an inflammatory response stimulated by adipocyte apoptosis. Inflammation peaks at approximately 14 days with as adipocytes are engulfed by histiocytes, neutrophils, lymphocytes and other mononuclear. Between 14 and 30 days' phagocytosis of the lipids is apparent macrophages and phagocytes surround and digest the contents of the dead cells, part of the natural injury response.

It is however interesting to note that the mechanism behind the cell death and elimination is not understood, initial studies have isolated adipocytes and exposed cells to temperatures between -2 and 28°c for 1 hour observing that between -2 and 7°c cells were necrotically injured regardless of recovery time, however between 14 and 28°c no necrotic injury was shown but the same amount of apoptotic injury was observed. Suggesting that the "mechanism of action responsible for adipocyte death is based on an event that triggers apoptosis"

Clinical studies – The clinical studies again employed the use of a Zeltiq system used in the dosimetry animal studies, tissue was drawn into a cup with moderate vacuum positioning the skin between two thermoelectric cooling elements and monitored/controlled by heat flux sensors, a gel is also applied for consistent thermal contact. The treatment uses a predetermined heat extraction rate and cycle duration of up to 60 minutes.

Evaluation of clinical studies demonstrated that the observed effects of cryolipolysis initially observed in animals was replicated in humans. Further studies analysed in this paper further concluded that cryolipolysis didn't effect nerve of liver function with the lack of adverse side effects demonstrating safety.

Areas for further research:
-How did the addition of tissue stimulation in the animal studies effect the results?
-More information on the settings used in each study.
-How to effectively measure skin temperature.

Summary Points of Interest:
-Between 14°c and 28°c no necrotic cell injury was seen however adipocyte apoptosis was still observed, suggesting that an event is responsible for cell apoptosis.

- The predetermined energy extraction rate mentioned in the clinical study, suggests that the TEC temperature fluctuates to keep the skin temperature constant but does not state the temperature used in the clinical studies. -The paper suggests that more research is required into the application of cryolipolysis to other parts of the body and the optimal parameters for each.

Title: Cryolipolysis for Fat Reduction and Body Contouring: safety and efficacy of current treatment paradigms	**Date**: 2014
Author: Michael J. Ingargiola M.D, Saba Motakef M.D, Michael T. Chung, Henry C M.D. Vasconez M.D, Gordon H. Sasaki M.D	**Category**: CryoB
Summary: A review paper exploring existing cryolipolysis studies and their outcomes focusing on human studies and finding the correlation between the selected studies.	
Findings: The research paper consisted of 319 primary sources of research systematically filtered papers based on the abstract, reference reviews and excluding animal papers, leaving a total of 19 articles considered in the publication of this paper. The reviewed papers had their Cohen Kappa coefficient calculated to assess agreement between articles resulting in a coefficient of 0.885 indicating a very strong agreement between the reviewed articles demonstrating cryolipolysis is a promising procedure for non-invasive fat reduction and body shaping, and identifying post treatment manual massage as having significant potential to improve the efficacy of cryolipolysis. The study highlighted several interesting studies to further explore in the references in relation to the operation of the machine ect, and show promise in helping define critical specification to the project. Other points raised in this study include the application of treatment to specific areas and the potential to create adaptive application for personalised treatment. Further to this the effects of multiple treatments was evaluated in a study concluding that being exposed to more than one session of cryolipolysis did show a reduction in the fat layer. Another point of discussion mentions the mechanism behind vacuum suction with regulated heat extraction, it's believed to impede blood flow and induce crystallization of targeted adipose tissue when cryolipolysis is performed, but there is no data on the benefits of vacuum suction and thus requires more research into this.	
Areas for further research: This paper includes many research articles used in this review and of significant relation to the Cryostim project thus should be highlighted and analysed. - The application of treatments to certain areas - Identifying parameters - Post treatment massage to best effects and how ems can replace manual massage	

Summary Points of Interest: - Study identified that there's significant potential to explore the benefits of combined cryocooling with post manual massage as an area for future research and innovation.

Title: Review of the mechanisms and effects of Noninvasive body contouring devices on cellulite and subcutaneous fat	**Date**: 26/06/16
Author: Zahra Alizadeh, Farzin Halabchi, Reza Mazaheri, Maryam Abolhasani and Mastaneh Tabesh	**Category**: CryoB
Summary: A review paper analysing multiple current treatments employed in reducing subcutaneous fat their measured results, safety and analysis	
Findings: The paper explored multiple methods of reducing subcutaneous fat, including radio frequency, low level laser therapy, high intensity focused ultrasound, whole body vibration and extracorporeal shockwave therapy and their distinct methods for stimulating adipocyte apoptosis. It became evident that the possibility to explore the combination of cryotherapy and electro muscle stimulation with additional treatments and the potential to further stack technologies. A document should be produced evaluating the methods of stimulation of each technology and reviewed against the method of stimulation cryolipolysis. The review confirms the findings on cryolipolysis from previous review papers however it raises more studies for further research into the mechanisms and ideals behind cryolipolysis. A point of interest raised in the discussion is that cryolipolysis is not dependant on the operator and this should be considered as an advantage, yet long treatment sessions are an important disadvantage.	
Areas for further research: - Studies used in the review paper. - Evaluate extracorporeal shockwave therapy	
Summary Points of Interest: - Cryolipolysis is not dependant on the operator - Possibility to combine with other subcutaneous fat reducing technology - Extracorporeal shockwave therapy	

Title: Effects of Cryolipolysis on Abdominal Adiposity	**Date**: 10/2016
Author: Patricia Froes Meyer, Rodrigo Marcel Valentim da Silva, Glenda Oliveira, Maely Azevedo da Silva Tavares, Melyssa Lima Medeiros, Camila Procopio Andrada and Luis Gonzaga de Araujo Neto	**Category**: CryoB

Summary: A case report to validate the effects of cryolipolysis in eliminating abdominal fat cells through apoptosis. The subject was a 46-year-old female participant with no contraindications to the use of cryolipolysis, furthermore the presence of abdominal fat and being in a preoperative period of abdominoplasty surgery were the aspects leading to the candidate's consideration for the study. The patient was submitted to a single 60-minute application of cryolipolysis at -5°C in the hypogastrium area, 5cm bellow the umbilicus, the patient was then analysed 7, 15, 30 and 45 days after initial treatment. After the abdominoplasty parts of the treated and untreated withdrawn abdominal tissue were evaluated macro- and microscopically.

Findings: The case study showed a reduction in the measured abdominal fat tissue both in ultrasound tests and physical measurement assessments indicating that the use of cryolipolysis on the abdominal can yield positive safe results.

This paper doesn't however provide much analysis into the optimal treatment parameters for the abdominal area, a further study using multiple patients at different cooling intensity factors would be beneficial in the optimisation of localised treatment sites.

Areas for further research:
- Machine Learning
- Other frequent sites of the body.

Summary Points of Interest:
Treatment parameters – Single application, lower abdomen, 60 minutes, suction pressure 60kPa at a temperature of -5°C

Title: Improved methods for selective cryolipolysis results in subcutaneous fat layer reduction in a porcine model	**Date**: May 2014
Author: T.-R. Kwon, K. H. Yoo, C.T Oh, D. H. Shin, E. J. Choi, S. J. Jung, H. Hong, Y. S. Choi an B. J. Kim	**Category**: CryoB

Summary:
A paper reviewing the improved selective cryolipolysis results in subcutaneous fat layer reduction in a porcine model using the CRYOLIPO II – This paper is an experimental study looking at the efficacy of the CRYOLIPO II machine on reducing abdominal adipose tissue in micro-pigs. The experiment was conducted on 2 micro-pigs exposed to 60 minutes at a cooling intensity factor of 24.9 (-44.68 mW/cm^2) followed by a massage that was performed automatically by the device for a period of 10 minutes.

Findings: The study concluded the that the CRYOLIPO II effectively resulted in fat layer reduction on the porcine model, however doesn't specify if any benefits were observed or not in the fat reduction of either pig due to the addition of a 10-minute post massage treatment.

The study also demonstrated the potential of using ultrasound to determine subcutaneous fat levels as well as thermal imaging techniques prior and post exposure and the use of 3d imaging in demonstrating skin contour changes.

In the results discussion, the cooling conditions were stated as -7°C however images of the treated surface area immediately after cryocooling show a skin surface temp of 16.4°C, therefore does the temperature of the part must account for extra work the body is doing to overcome the cold stimulus?
Areas for further research:
Summary Points of Interest: - CRYOLIPO II Machine used in experiment

Title: Cryolipolysis conformable-surface applicator for nonsurgical fat reduction in lateral Thighs	**Date**: 12/6/2014
Author: W. Grant Stevens, MD, Eric P. Bachelor, MD, FACS	**Category**: CryoB
Summary: A paper reviewing the efficacy of a prototype conformable-surface Cryolipolysis applicator (Coolsmooth Applicator, cool sculpting system, Zeltiq Aesthetics) the treatment methodology in question features a vacuum suction cup pinching skin between the two cooling panels regulated by a standardised cooling intensity factor. The case study evaluated the both the safety and efficacy of this as a 120-minute treatment as opposed to standardised treatment times of 60 minutes.	
Findings: The study concluded that the application of the Coolsculpting prototype to the treatment area (lateral Thighs) resulted in safe and efficacious reduction in the subcutaneous fat layer. The study used 2D ultrasound measurement to quantify fat layer reduction, would it be feasible to employ 2D ultrasound into the Cryostim project to measure the layer of adipose tissue? This would allow increased accuracy when compared to traditional calliper measurements. The study also acknowledges that a limitation is it was performed on a single participant, further to this the paper identifies the potential benefits of multiple treatments being beneficial throughout a prolonged treatment plan. A further issue raised in the paper was the inconvenience and impracticality of the treatment to the patient as not being able to reposition themselves throughout the two-hour exposure and thus may increase stress levels, being counter-productive to the treatment. One of the key topics for discussion is the application of the prototype to fibrous areas I.e areas of the body which do not lend themselves to the conventional paradigms of treatment, limiting the suitable candidate for Cryolipolysis to a very select few which fit within the boundaries. This paper was funded by Zeltiq, low cost single participant study to prove their approach works.	
Areas for further research: - 2D Ultrasound technology	
Summary Points of Interest:	

- 2D Ultrasound as possible method of measuring layers of adipose tissue.
- Identified points of interest include multiple treatments of one singe area as part of a treatment plan for further fat reduction.
- The inconvenience of having a machine applied to the treatment area for a prolonged period.
- Identification that the treatment is not ideal for all patients and patients are required to have a fat layer measurement falling between certain figures to be suitable for vacuum cryolipolysis.

Title: Anthropometric Characteristics and sex influence magnitude of skin cooling following Exposure to whole body cryotherapy	**Date**: 2014
Author: L.E Hammond, S. Cuttell, P. Nunley and J. Mayer	**Category**: CryoB

Summary: This paper explores the differences in anthropometric characteristics and sex influence in whole body cryotherapy. This is the first paper I've read exploring how variables in the adipose layer can affect the efficacy of treatment further to this the paper compares the results of both male and female participants to determine the role of sex in adipose apoptosis.

Further to this the study looks to examine if anthropometric measures can be used to predict the extent of fat loss. An interesting concept which opens door to machine learning and personalisation of treatment based on both anthropometrics and sex

Findings: One of the findings discussed early in the paper suggest that the thickness of adipose tissue affects cooling time and goes on to state that this is because thicker skinfolds require longer ice exposure than thinner skinfolds to reach a standard temp in deep tissue. Further to this suggesting that there is a current lack of research into the treatment across multiple areas.

The study used thermal imaging to not interfere with the skin temperature.

The study went on to confirm a positive correlation between body fat and temperature at skin level, further to this identifying that females cooled more than males.

Another interesting topic discussed in the paper was the anatomical location of application with lower extremities showing a greater change in temperature. This point could further prove blood flow counteracting cooling in Cryotherapy procedures.

This paper is of interest proving potential significance of further studies into the benefits of machine learning in relation to the project and developing personalised adaptive treatment.

Areas for further research:
- Differences in adipose tissue thickness and relative cooling efficiency
- Machine Learning in medicine
- Anatomical differences in blood flow

Summary Points of Interest: This paper is of significant interest

Title: Effects of Cryotherapy, transcutaneous electrical stimulation and their combination on femoral nerve electrical activity in nerves	**Date**: 2008
Author: Satuzzi CH, Goncalves WLS, Rocha SS, Castro MEC, Gouveia SA	**Category**: CroB/EMSB
Summary: A study of the onset effects of combined cryocooling and electro muscle stimulation in stimulating analgesia (pain relief) Based on the understanding that both cryocooling and EMS can induce analgesia alone, the combination of both treatments was to be explored in this study to observe the effects on femoral nerve activity in rats.	
Findings: The study firstly identifies the treatment parameters for Transcutaneous electro nerve stimulation and the effects of different intensities before identifying the correct intensity for the treatment, this point lead to thinking about firstly how this could apply to machine learning and secondly establishing different combined treatment parameters for different required treatments, i.e setting the tens machine to more intensive shocking to contract muscle and stimulate blood flow or light continuous muscle contractions to exploit the pain relief potential. Thus the equipment used in the programming must be variable. Reading further into the paper another point of interest made clear was the current application of combined treatment being used in hospitals in patients experiencing pain post operation, thus establishing potential for a medical hospital market. The electroneurographic results obtained indicate the sequential use of tens and cryo can improve the analgesic pattern. A final note on the newly observed pattern of FNA in combined treatment should mean for caution to be taken in further studies.	
Areas for further research:	
Summary Points of Interest: - Potential for product in medical hospital market - The applications of TENS for different treatments - Caution with combining TENS and CRYO as a new pattern of FNA response was observed	

Title: Full-thickness wounds resulting from do-it-yourself cryolipolysis: a case study	**Date**: April 2016
Author: C.D. Leonard, S.A Kahn, J.B Summitt	**Category**: CryoB
Summary: A report reviewing the case of a 55-year-old woman who suffered frost bite whilst attempting DIY cryolipolysis without the guidance or supervision of a medical professional. Using Dry Ice as a medium of cooling after having read online instructional tutorials.	
Findings: The paper explores a growing phenomenon of internet enabled research into methods of self-treatment and the reported consequences of doing so.	

The case in question is of a 55-year-old female who proceeded to self-administer cryolipolysis having watched YouTube videos describing how to do it yourself. The patient claimed to have wrapped dry ice in a paper bag and saran wrap, proceeding to lay on top of it rotating the packing along the four quadrants of the abdomen in 15 minute intervals, after the last application she reported that she felt 'frozen and numb' resulting in substantial cooling wounds. In the papers discussion, the cause of the issue is said to be temperatures far cooler than the recommended cryolipolysis temperatures, with the temperature of dry ice being -78°C whilst the temperatures for cryolipolysis generally stay about -7°C The report goes onto identify a range of methods of self-treatment documented through how to guides and tutorials available readily online, ranging from primitive methods such as wrapping ice in a towel in YouTube videos to more advanced detailed schematics for building a cryocooling machines, (it may be beneficial to find this guide)
Areas for further research: Research and review guides and online DIY treatment content - Frankensculptor - Coolsculpting at home for less than $5 - CoolSculptingAtHome Think about how to prevent people from attempting to administer the treatment themselves.
Summary Points of Interest: Strategies to prevent such injury should be developed on a national scale General cryolipolysis acting temperatures -7°C

Title: On-Site Thermoelecric Cooling Device for Cryotherapy and Control of Skin Blood Flow	**Date**: 12/2015
Author: Natalia Mejia, Karl Dedow, Lindsey Nguy, Patrick Sullivan, Sepideh Khoshnevis, Kenneth R. Diller	**Category**: CryoT
Summary: A Paper documenting the research into the application of thermoelectric modules and their efficiency in cooling to required therapeutic cryocooling temperature.	
Findings: The project concluded that Thermoelectric cooling modules could provide sufficient cooling to allow the delivery of the required treatment parameters.	
Areas for further research:	
Summary Points of Interest:	

Title: The use of Cryotherapy in Acute Sports Injuries	**Date**: 25/02/16
Author: Leonarda Galiuto	**Category**: CryoB

Summary:
A paper analysing and describing the scientific evidence supporting the therapeutic value of cryotherapy based on the outcome analysis.

The paper reviews 52 published articles on the topics of acute sports injury and cryotherapy aiming to propose the most validated method of application based on published data.

Findings:
Although a definitive conclusion on the efficacy of cryotherapy cannot be drawn based on current evidence; the consensus is to continue to use cold therapy soon after acute sports injury and their surgical treatment.

Cooling results in heat loss, the treated body area experiences vasoconstriction, decrease in inflammatory reaction and relative symptoms.

The paper identifies cytotherapeutic agents to have a pre- application temperature range between 10 to 15°C

Ideal treatment duration and frequency not yet defined; ranging from 10-20 minutes 3 to 4 times per day, or 30-45 minutes every 2 hours. At present there is no evidence as to which method is most effective or whether it should be used intermittently or continuously.

Optimal tissue temperature reduction of 10 to 15°C may be necessary in order to achieve local analgesia and lower metabolism.

Identifies that the addition of ice to compression is more effective than compression alone.

Areas for further research:

Summary Points of Interest:
-Pre- application temperature identified as between 10-15°C for treatment of acute injury.
-States that the most effective mode of cryotherapy is not yet known.
-Identifies that each therapy should only be provided to a patient only if supported by scientific research.
-Identifies the addition of ice to compression as more effective than that of ice alone.

Title: Motor and Sensory Nerve Conduction Are Affected Differently by Ice Pack, Ice Massage, and Cold Water Immersion	**Date**: 2010
Author: Esperanza Herrera, Maria C. Sandoval, Diana M. Camargo, Tania F. Salvini	**Category**: CryoB

Summary: This paper compares different cooling applications and how they affect nerve conduction parameters. Comparing ice pack, ice massage and cold water immersion.
Findings: The study found that cold water immersion was most indicated modality for inducing therapeutic effects associated with a reduction of motor nerve conduction. The researchers observed that this could be due to water immersion covering a larger area than the ice pack or ice massage.
Areas for further research: Research into whole body water submersion.
Summary Points of Interest: Cold Water Submersion identified as providing best therapeutic effects.

Title: Subcutaneous Adipose Tissue Thickness Alters Cooling Time During Cryotherapy	**Date**: 2002
Author: Jeffrey W. Otte, MS, Mark A. Merrick, PhD, Christopher D. Ingersoll, PhD, Mitchell L. Cordova, PhD	**Category**: CryoB
Summary: This paper looked to determine if differing subcutaneous adipose thickness alters the treatment duration required to produce a standard cooling effect during Cryotherapy.	
Findings: It was observed that cooling time increased as adipose thickness increased. The results indicate that a dramatic adjustment to cryotherapy duration is required to produce similar IM temperature changes. "A 25 minute treatment may be adequate for a patient with a skinfold of 20mm or less; however, a 40 minute application is required to produce similar results in a patient with skinfolds between 21-30mm, whereas a 60-minute application is required for patients with skinfolds of 30 to 40mm."	
Areas for further research:	
Summary Points of Interest: cooling time increased as adipose thickness increased	

Title: The Relationship Between Intramuscular Temperature, Skin Temperature, and Adipose Thickness During Cryotherapy and Rewarming	**Date**: 2001
Author: Lisa S. Jutte, MS, Mark A. Merrick, PhD, Christopher D. Ingersoll, PhD, Jeffrey E. Edwards, PhD	**Category**: CryoB

Summary: To describe the relationships among muscle temperature, skin temperature, room temperature, body core temperature, time, and subcutaneous adipose thickness during cryotherapy and rewarming.
Findings: Skin surface temperature was a weak predictor of IM temperature during cryotherapy and should not be used as the sole dependant measure in cryotherapy efficacy studies.
Areas for further research:
Summary Points of Interest: Skin surface temperature is a poor indicator of intramuscular temperature.

Title: Treatment of the Inversion Ankle Sprain: Comparison of Different Modes of Compression and Cryotherapy	**Date**: 1993
Author: Gary B. Wilerson, EdD, ATC, Helen M. Horn-kingery, Med, PT	**Category**: CryoB
Summary: The study reviewed existing Cryotherapy products to determine if a particular application gave improved results. The applications included compression and compression with ice pack.	
Findings: Typical cryotherapy procedure applied in one or two daily sessions. It was observed that an application of external compression has a greater effect on the rate of restoration of function than does the frequency and duration of Cryotherapy.	
Areas for further research:	
Summary Points of Interest: Application of external compression has a greater effect on the rate of restoration of function.	

Title: Cold-Water immersion and other forms of cryotherapy: physiological changes potentially affecting recovery from high-intensity exercise	**Date**: 2013
Author: Gillian E White, Greg D Wells	**Category**: CryoB
Summary: The paper provides a review of the acute physiological changes induced by various cryotherapy modalities that may affect recovery in the hours to days that follow high intensity exercise.	
Findings: Although the types of treatment are commonly used to speed recovery from stressful bouts of exercise there are no standard guidelines for procedures and a target temp for optimal effects identified.	

Physiological changes induced by cryotherapy may have a role in recovery from exercise, however studies are currently unable to identify if cryotherapy has a role greater than placebo on recovery. Whole Body Cryotherapy shows no performance differences reported post procedure.
Areas for further research:
Summary Points of Interest: Exercise there are no standard guidelines for procedures and a target temp for optimal effects identified.

Title: Cryotherapy – An Inevitable part of Sports Medicine and its benefits for Sports Injury – International Journal of Applied Research	**Date**: 2015
Author: Dinesh Saini	**Category**: CryoB
Summary: Explores the critical temperature application of cold in relation to motor performance, inflammation and oedema.	
Findings: Optimum motor performance temperature defined at 18°C, above and beneath muscle performance decreases. Critical temperature for the application of cold with inflammation and oedema increasing at temperatures below 15°C. Precautions should be taken because prolonged application at very low temperatures could have deleterious effects. The main concern with cryotherapy is keeping temperature within a specific range, so that very low temperature treatments are avoided – too cold a therapy can cause serious side effects inc nerve damage and frost bite. Combination of compression and cold highlighted as more effective than single cold application.	
Areas for further research:	
Summary Points of Interest: - Critical temperature for the application of cold with inflammation and oedema increasing at temperatures below 15°C - Precautions should be taken because prolonged application at very low temperatures could have deleterious effects.	

Title: Comparing the Antiswelling and Analgesic Effects of Three Different Ice Pack Therapy Durations: A Randomised Controlled Trial on Cases With Soft Tissue Injuries	**Date**: 2013

Author: Chai-Chi Kuo, Chiu-Chu Lin, Wei-Jing Lee, Wei-Ta Huang	**Category**: CryoB
Summary: The study explored the antiswelling and analgesic effects of different ice pack therapy durations on soft tissue injuries as well as discomfort.	
Findings: The study found no significant differences in the effect of different ice pack therapy durations. The paper recommends 10 minutes as the optimal ice pack therapy duration for soft tissue injuries. The paper identifies a mean reduction in skin temperature of 9-10°C	
Areas for further research:	
Summary Points of Interest: The paper identifies a mean reduction in skin temperature of 9-10°C	

Title: The Effect of Post-Exercise Cryotherapy on Recovery Characteristics: A Systematic Review and-Meta Analysis	**Date**: 2015
Author: Erich Hohenauer, Jan Taeymans, Jean-Peirre Baeyens, Peter Clarys, Ron Clijsen	**Category**: CryoB
Summary: A meta-analysis critically determining the possible effects of different cooling applications and strategies.	
Findings: Cryotherapy techniques have been used for decades. There was no evidence, that cooling affects any objective recovery variable in a significant way during a 96 hrs recovery period. Cold air temperature used in one localised cryotherapy study -30°C Advised to take the thickness of adipose into account as can significant effect the rate of cooling in procedures. Identifies the need to explore an algorithm for calculating the ideal cooling temperature, respectively cooling duration for specific amounts of adipose tissue. Cold air applications probably do not cool as deep as cold applications with direct contact to skin, and only effect skin temperature. Studies should consider the use of cheap and mobile cooling equipment, because it might clinically be more relevant for an advisor to use such devices compared to fixed / expensive cooling devices.	

Areas for further research: Bleakley et al – Claimed (2012) cryotherapy techniques used in humans do not sufficiently cool tissue to produce any physiological effects.
Summary Points of Interest: Real all points - Very good paper

Title: Effects of Air-Pulsed Cryotherapy on Neuromuscular Recovery Subsequent to Exercise-Induced Muscle Damage	**Date**: 2013
Author: Gae l Guilhem, PhD, Francxois Hug,z PhD, Antoine Couturier, PhD, Ste´ phanie Regnault, MSc, Laure Bournat, MSc, Jean-Robert Filliard, PhD, and Sylvain Dorel, PhD	**Category**: CryoB
Summary: The randomised controlled trail aimed to determine the effects of cold air local cryotherapy on recovery time of neuromuscular function following strenuous eccentric exercise.	
Findings: The study found that although symptoms of injury were delayed following a cryotherapy session the procedure the study provides evidence that the cooling procedure failed to improve long term recovery of muscle performance. Outline of a procedure 3 x 4min at -30°C separated by 1 min interval.	
Areas for further research:	
Summary Points of Interest: Outline of a procedure 3 x 4min at -30°C separated by 1 min interval	

Title: Transcutaneous Electrical Nerve Stimulation (Tens): A Technology Assessment	**Date**: 1996
Author: Janis Reeve, Devidas Menon, Paula Corabian	**Category**: EMSP
Summary: The paper assesses the effectiveness of TENS and scientific evidence for treatment of acute, chronic, labour and delivery pain. Addresses the uses of the technology in hospitals.	
Findings: The paper concludes that there is little evidence for other than a limited use of TENS. The paper has a good insight on the history of TENS. Concludes that TENS is a wasteful procedure if its optimum use has not been identified.	
Areas for further research:	
Summary Points of Interest: The paper has a good insight on the history of TENS	

Title: Effects of transcutaneous electrical nerve stimulation on pain, walking function, respiratory muscle strength and vital capacity in Kidney donors: a protocol of randomised controlled trial	**Date**: 2013
Author: Thiago Galli, Luciana Dias Chiavegato, Nathalia Risso Santiago, Richard Eloin Liebano	**Category**: EMSP
Summary: The paper looks to evaluate the effects of TENS in donor population, looking into pain relief and improvement in pulmonary tests and mobility.	
Findings: The paper outlines a setting for the administration of TENS at 100 Hz pulse duration 100 microseconds for 1 hour.	
Areas for further research:	
Summary Points of Interest:	

Title: A Low Cost Electrical Muscle Stimulation Device for Biomedical Applications	**Date**: 2014
Author: Samir Boukhenous, Adel Touchen, Mohamed Kourbeb, Zineb Raissi, Mokhtar Attari	**Category**: EMST
Summary: The paper looks at the development of a Unit for EMS procedures and outlines the settings for it to deliver for biomedical applications.	
Findings: Paper only documents the design of the stimulator and not the settings for procedures.	
Areas for further research:	
Summary Points of Interest:	

Title: Electrical Stimulation for Chronic non-specific low back pain in a working-age population: a 12-week double blind randomized controlled trail	**Date**: 2013
Author: Matthew S Thiese, Matthew Hughes, Jeremy Biggs	**Category**: EMSP
Summary: The study compares TENS to Sham TENS to determine comparative efficacy for treatment of chronic non-specific back pain.	

Findings: 1-70 Hz duration of 5 milliseconds Notes minimal improvements to sham TENS – Funded by TENS company
Areas for further research:
Summary Points of Interest:

Title: A Controlled trail of Transcutaneous Electrical nerve stimulation (tens) and exercise for chronic low back pain	**Date**: 1990
Author: Deyo RA, Walsh NE, Martin DC, Schoenfeld LS, Ramamurthy S.	**Category**: EMSP
Summary: Aimed to conclude the efficacy of TENS procedures for chronic back pain using 9V take home units 45 mins three times a day. The study concluded TENS no more effective than treatment with placebo.	
Findings: The settings for lower back pain were 80-100 pulses per second at an amplitude of 30 Hz Secondary setting 2-4 pulses per second at an amplitude of 100 Hz	
Areas for further research:	
Summary Points of Interest: were 80-100 pulses per second at an amplitude of 30 Hz 2-4 pulses per second at an amplitude of 100 Hz	

Title: Transcutaneous electrical nerve stimulation for the management of tennis elbow: a pragmatic randomised controlled trial: the TATE trail	**Date**: 2009
Author: Chesterton LS, van der Windt DA, Sim J, Lewis M, Mallen CD, Mason EE, Warlow C, Vohora K, Hay EM.	**Category**: EMSP
Summary: The study aims to explore the efficacy, cost and pain relief in the self-management package of TENS.	
Findings: 110 Hz with a pulse duration of 200 microseconds	
Areas for further research:	
Summary Points of Interest:	

Title: Effect of transcutaneous electrical nerve stimulation on pain intensity in reduced consciousness patients: a randomised trail	**Date**: 2017
Author: Maryam Jalalmanesh, Shahin Heidari, Majid Kazemi, Farshid Rahimi-Bashar, Hamid-Reza Rostami	**Category**: EMSP
Summary: A study on the effect of TENS on pain intensity followed by surgery in patients hospitalised in intensive care units.	
Findings: Definition of conventional TENS – 80 Hz at 330 microsecond – subset of High TENS setting	
Areas for further research:	
Summary Points of Interest:	

Title: Does Electrical Stimulation enhance post-exercise performance recovery?	**Date**: 2011
Author: Nicolas Babault, Carole Cometti, Nicola A Maffiuletti, Graelle Deley	**Category**: EMSP
Summary: A paper reviewing the efficacy of TENS on post exercise recovery. Aims to clarify the effectiveness of electrical stimulation as a recovery modality.	
Findings: Outlines of Different procedure parameters – 30 Hz, 120 Hz, 4 Hz, 110 Hz, 120 Hz, 5 Hz Duration – 40, 200, 200, 100, 250 Microsecond Low Frequency <10 Hz High intensity stimulations = visible muscle contractions High Frequency (50-100 Hz) low intensity = Strong but comfortable without muscle contractions	
Areas for further research: Effect of Transcutaneous Electrical Nerve Stimulation, Cold, and a Combination Treatment on Pain	
Summary Points of Interest:	

Title: Effect of Transcutaneous Electrical Nerve Stimulation, Cold, and a Combination Treatment on Pain, Decreased Range of Motion, and Strength Loss Associated with Delayed Onset Muscle Soreness	**Date**: 1992
Author: Craig R. Denegar, PhD, ATC and David H. Perrin, PhD, ATC	**Category**: EMSP
Summary: The study observed changes in perceived pain following a procedure combining cryotherapy with TENS.	
Findings: The study used a pulse rate of 90 pps duration of 90 u sec A second setting of 2pps phase duration of 20 u sec intensity @110ma The study showed that combination of TENS with cold or TENS and cold had greater effects on pain than just cold or TENS – The methods used an ice pack over electrodes – intramuscular temperature was not measured however it's proposed at 18°C at 15 minutes and 11°C at 22 mins.	
Areas for further research: How does compression effect this?	
Summary Points of Interest:	

Title: Comparing the Effects of Cryotherapy and Transcutaneous Electrical Nerve Stimulation on Signs and Symptoms of Delayed Onset muscle soreness in amateur Athletes	**Date**: 2017
Author: Kazim malmir, Nastaran Ghotbi, Seyed Mohsen Mir, Behzad Moradi	**Category**: CryoB
Summary: Comparing the effects to TENS and Cryotherapy to DOMS	
Findings: The paper shows that Cryotherapy was more effective than TENS for controlling pain. Settings – 110 Hz, 200 u sec for 20 mins.	
Areas for further research:	
Summary Points of Interest:	

Title: Effects of Cryotherapy, Transcutaneous electrical stimulation and their combination on femoral nerve activity in rats	**Date**: 2008
Author: Satuzzi CH, Goncalves WLS, Rocha SS, Castro MEC, Gouvea SA, Abreu GR	**Category**: CryoB
Summary: A study looking at the effects of a combined procedure on femoral nerve activity in rats	

Findings: Researchers found that the combination significantly attenuated the effects produced by TENS alone on nerve activity. Studies show intensities for TENS between 10 and 30 milliamperes are more comfortable and don't cause significant fasciculation in the pulse time, varying from 40 to 75 u Sec.
Areas for further research:
Summary Points of Interest: TENS between 10 and 30 milliamperes are more comfortable

Title: Effects of transcutaneous electrical nerve stimulation and cryotherapy on pain threshold by induced pressure	**Date**: 2014
Author: Lairton Fabricio de Menezes Maciel, Jose Jamacy de Almeida Ferreira, Heleodorio Honorato dos Santos, Palloma Rodrigues de Andrade	**Category**: Cryob
Summary: Investigating TENS and Cryo independently and together and its effects on pain management	
Findings: The study concluded cryotherapy alone as the best mode for reducing pain. Tens settings – 100 Hz and 40 u sec	
Areas for further research:	
Summary Points of Interest:	

Title: Analgesic effectiveness of the association of transcutaneous electrical nerve stimulation and cryotherapy for chronic low back pain	**Date**: 2011
Author: Eliziete Almeida de Abreu, Jean Douglas Moura dos Santos, Patricia Lima Ventura	**Category**: CryoB
Summary: Paper investigates the combination of TENS and Cryo on pain thresholds	
Findings: Combination showed no significant improvement as compared to isolated procedures Settings used – 100 Hz duration 150 U sec	
Areas for further research:	
Summary Points of Interest:	

Title: Effect of Burst TENS and conventional TENS combined with cryotherapy on pressure pain threshold: Randomised, controlled, clinical trial	**Date**: 2015
Author: L.B. Macedo, A.M. Josue, P.H.B. Maia, A.E Camara, J.S. Brasileiro	**Category**: EMSP
Summary: To assess the immediate effect of TENS in combination with Cryotherapy on pain threshold and tolerance on heathy individuals	
Findings: The paper shows the combination of burst TENS to have a greater effect in combination with cryotherapy than standard TENS on induced pain. Settings – low frequency high intensity – 80-100 Hz modulated in low freq pulse trains 2 – 5 Hz long pulse duration 150 u sec.	
Areas for further research:	
Summary Points of Interest:	

Title: Does transcutaneous electrical nerve stimulation (TENS) simultaneously combined with local heat and cold applications enhance pain relief compared with TENS alone in patients with knee osteoarthritis?	**Date**: 2017
Author: Takaya Maeda, RPT, MS, Hideki Yoshida, RPT, PhD, Tomoyuki Sasaki, MD, PhD, Atsushi Oda RPT, PhD	**Category**: EMSP
Summary: The study explored the combination of TENS heat and Cryo to enhance pain relief.	
Findings: Study used 40°C as the temperature for local heat application TENS = 100pps frequency, 200 u sec pulse width, 20 minute stimulation duration. The study concluded that the TENS simultaneously applied with local heat or cold does not enhance pain relief of knee pain during standing or walking in patients with knee OA.	
Areas for further research:	
Summary Points of Interest:	

Title:	**Date**:
Author:	**Category**:
Summary:	